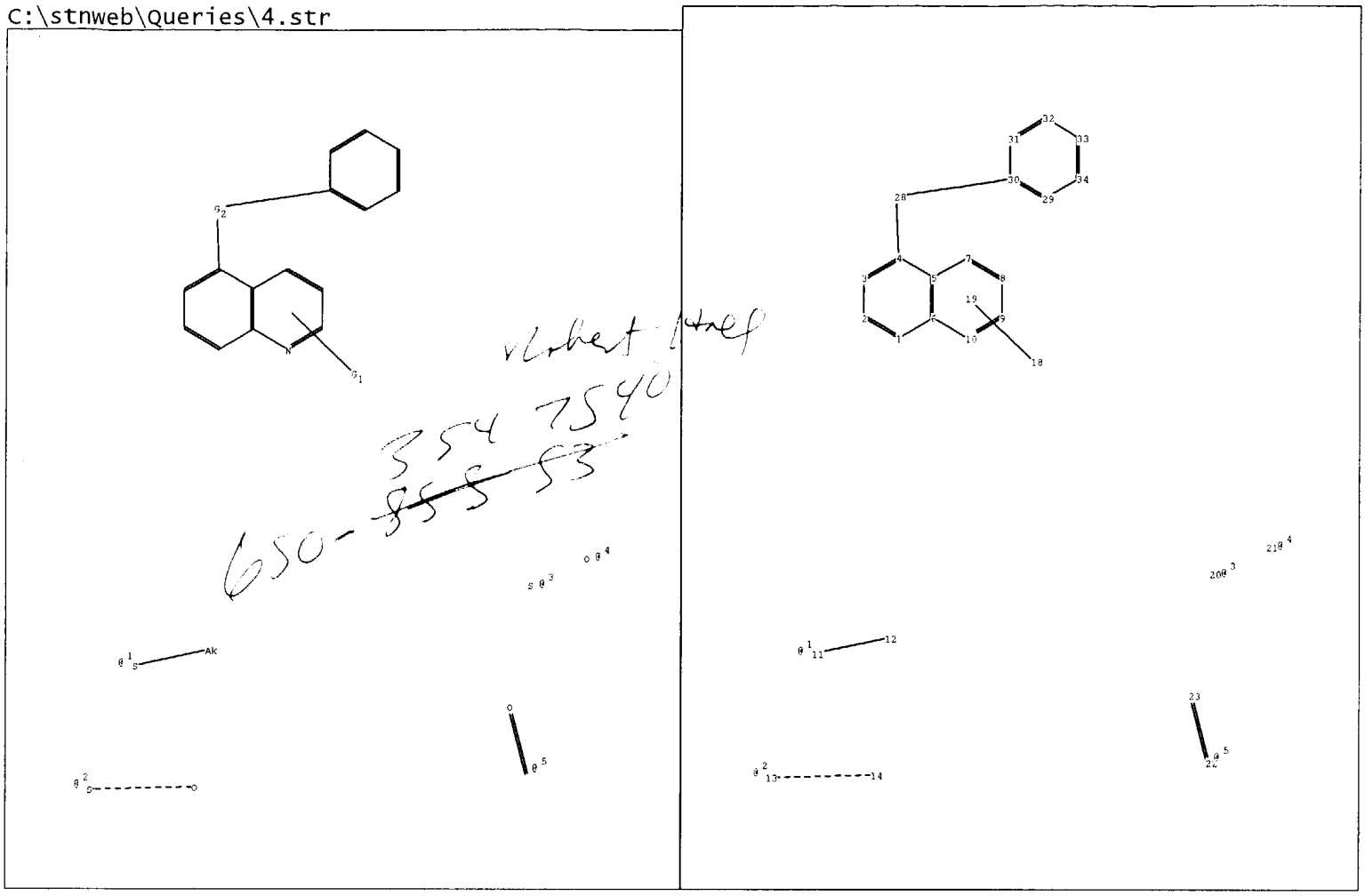
C:\stnweb\Queries\4.str



chain nodes :
11 12 13 14 18 20 21 22 23 28
ring nodes :
1 2 3 4 5 6 7 8 9 10 29 30 31 32 33 34
chain bonds :
4-28 11-12 13-14 22-23 28-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 29-30 29-34 30-31 31-32
32-33 33-34
exact/norm bonds :
4-28 11-12 13-14 22-23 28-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 29-30 29-34 30-31 31-32
32-33 33-34
isolated ring systems :
containing 1 : 29 :

G1:[*1],[*2]

G2:CH2,[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 14:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS
28:CLASS 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom

```
* * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  May 10   PROUSDDR now available on STN
 NEWS  4  May 19   PROUSDDR: One FREE connect hour, per account, in both May
                   and June 2004
 NEWS  5  May 12   EXTEND option available in structure searching
 NEWS  6  May 12   Polymer links for the POLYLINK command completed in REGISTRY
 NEWS  7  May 17   FRFULL now available on STN
 NEWS  8  May 27   New UPM (Update Code Maximum) field for more efficient patent
                   SDIs in CAplus
 NEWS  9  May 27   CAplus super roles and document types searchable in REGISTRY
 NEWS 10  May 27   Explore APOLLIT with free connect time in June 2004
 NEWS 11  Jun 22   STN Patent Forums to be held July 19-22, 2004
 NEWS 12  Jun 28   Additional enzyme-catalyzed reactions added to CASREACT
 NEWS 13  Jun 28   ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG,
                   and WATER from CSA now available on STN(R)

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   29 JUN 2004  HIGHEST RN 701199-61-3
DICTIONARY FILE UPDATES:  29 JUN 2004  HIGHEST RN 701199-61-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
```

conducting SmartSELECT searches.

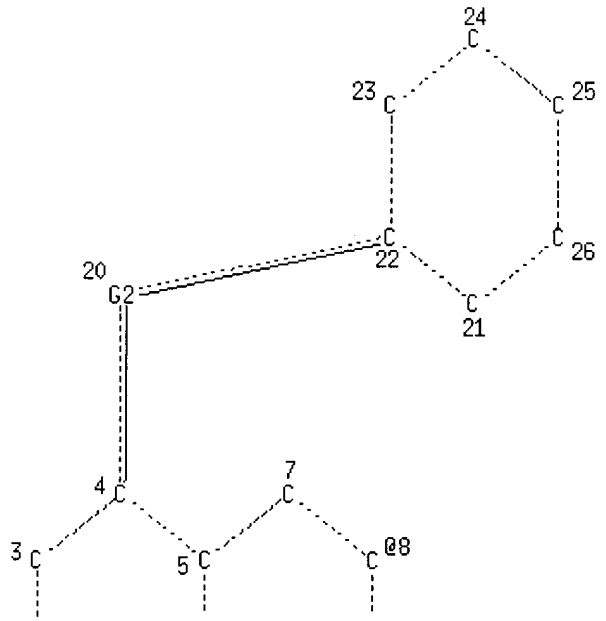
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

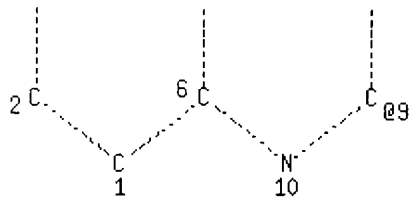
=>
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

27 C M2
Page 1-A

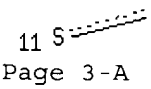


Page 1-B

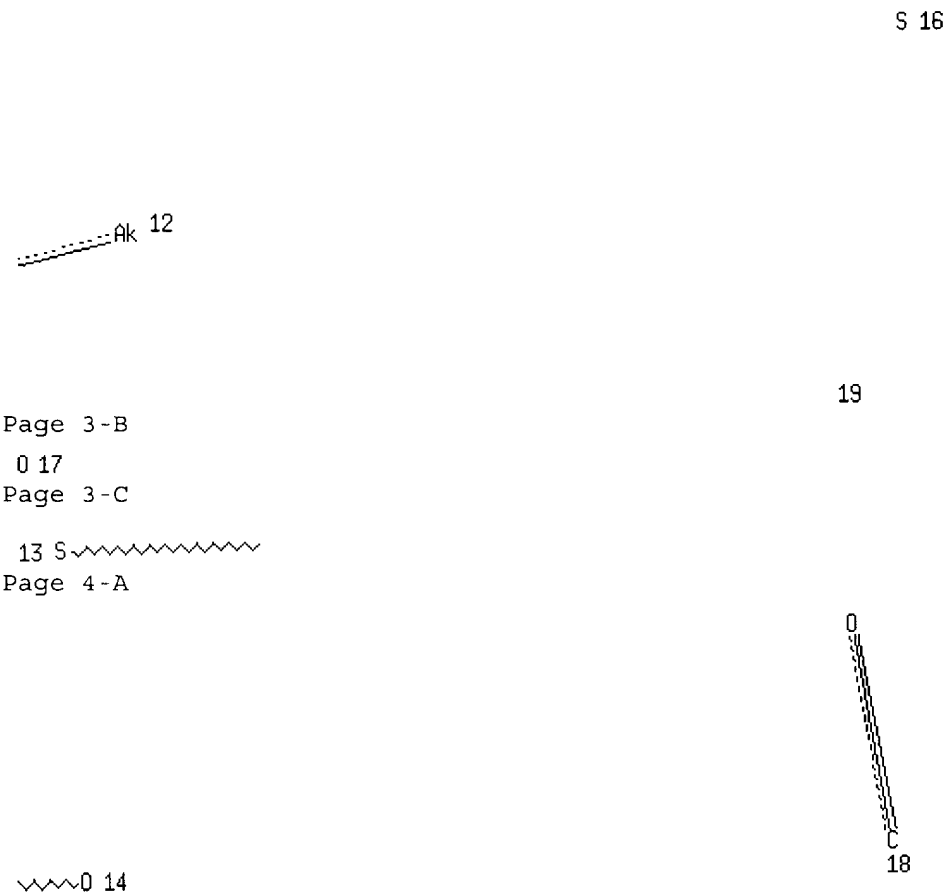


G1 @15

Page 2-B



Page 3-A




```
VAR G1=11/13
VAR G2=27/11-22 11-4/13-22 13-4/16-22 16-4/17-22 17-4/18-22 18-4
VPA 15-8/9 S
NODE ATTRIBUTES:
HCOUNT  IS M2     AT  27
NSPEC   IS R      AT   1
NSPEC   IS R      AT   2
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS R      AT   7
NSPEC   IS R      AT   8
NSPEC   IS R      AT   9
NSPEC   IS R      AT  10
NSPEC   IS C      AT  11
NSPEC   IS C      AT  12
NSPEC   IS C      AT  13
NSPEC   IS C      AT  14
NSPEC   IS C      AT  15
NSPEC   IS C      AT  16
NSPEC   IS C      AT  17
NSPEC   IS C      AT  18
NSPEC   IS C      AT  19
NSPEC   IS C      AT  20
NSPEC   IS R      AT  21
NSPEC   IS R      AT  22
NSPEC   IS R      AT  23
NSPEC   IS R      AT  24
```

```
NSPEC   IS R      AT  25
NSPEC   IS R      AT  26
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  11 12 13 14 16 17 18 19 27
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  27

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 13:38:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    358 TO ITERATE

100.0% PROCESSED     358 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         6025 TO     8295
PROJECTED ANSWERS:               3 TO      163

L2             3 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:38:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   6697 TO ITERATE

100.0% PROCESSED    6697 ITERATIONS                               52 ANSWERS
SEARCH TIME: 00.00.01

L3            52 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   162.14     162.35

FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 30 Jun 2004  VOL 141 ISS 1
```

FILE LAST UPDATED: 29 Jun 2004 (20040629/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 1 L3

=> d l4, ibib abs fhitstr, 1

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

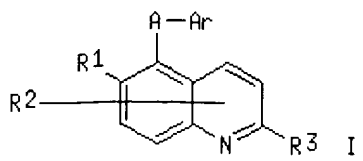
Full Text | Citing References

ACCESSION NUMBER: 2002:122959 HCAPLUS
DOCUMENT NUMBER: 136:183715
TITLE: Preparation of quinoline derivatives as antiinflammatory agents
INVENTOR(S): Broka, Chris Allen; Kim, Woongki; McLaren, Kevin Lee; Smith, David Bernard
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012192	A1	20020214	WO 2001-EP8880	20010801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001077560	A5	20020218	AU 2001-77560	20010801
EP 1313707	A1	20030528	EP 2001-955382	20010801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013175	A	20040217	BR 2001-13175	20010801
JP 2004505951	T2	20040226	JP 2002-518170	20010801
US 2002082276	A1	20020627	US 2001-925883	20010807

PRIORITY APPLN. INFO.: US 2000-224196P P 20000809
WO 2001-EP8880 W 20010801

OTHER SOURCE(S): MARPAT 136:183715
GI



I

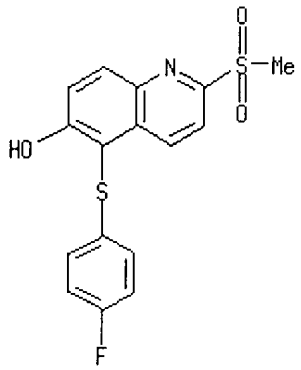
09/925883

AB The title compds. I [A = S, etc.; Ar = (un)substituted phenyl; R1 = H, alkoxy, etc.; R2 = H, alkyl, etc.; R3 = SO2R12, etc.; R12 = alkyl, etc.] are prepd. I are useful as inhibitors of COX-II and, therefore, may be used for the treatment of a disease treatable by administration of a selective COX-II inhibitor, such as an inflammatory disease, autoimmune disease. Processes for prepg. I are claimed. 5-(2,4-Difluorophenylsulfanyl)-2-methanesulfonyl-6-methoxyquinoline in vitro showed IC50 values of >40 μM and <0.2 μM against COX-I and COX-II, resp. Formulations are given.

IT **398456-42-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of quinoline derivs. as antiinflammatory agents)

RN 398456-42-3 HCAPLUS

CN 6-Quinolinol, 5-[(4-fluorophenyl)thio]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.12	169.47

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.69	-0.69

FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

```
=> d his

     (FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1              STRUCTURE UPLOADED
L2            3 S L1
L3           52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4            1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004

=> s l3
L5            0 L3

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       4.62     174.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -0.69

FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 30 Jun 2004  VOL 141 ISS 1
FILE LAST UPDATED: 29 Jun 2004  (20040629/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s cox-II () inhibitor?
         13950 COX
             2 COXES
         13952 COX
                 (COX OR COXES)
       1975477 II
           776 IIS
```

```
       1975918 II
                 (II OR IIS)
           172 COX-II
                 (COX(W)II)
        883030 INHIBITOR?
L6          32 COX-II (W) INHIBITOR?

=> s cox-2 () inhibitor?
         13950 COX
             2 COXES
         13952 COX
                 (COX OR COXES)
       8079364 2
          6672 COX-2
                 (COX(W)2)
        883030 INHIBITOR?
L7        2445 COX-2 (W) INHIBITOR?

=> s l7 or l6 and myositis?
           769 MYOSITIS?
L8        2447 L7 OR L6 AND MYOSITIS?

=> s l7 or myositis?
           769 MYOSITIS?
L9        3199 L7 OR MYOSITIS?

=> s l7 and myositis?
           769 MYOSITIS?
L10         15 L7 AND MYOSITIS?

=> s l10 and review/dt
       1738344 REVIEW/DT
L11           0 L10 AND REVIEW/DT

=> d l10, ibib abs, 1-2

L10  ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

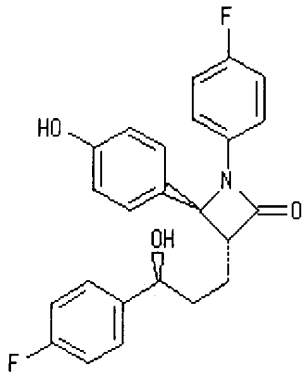
```
ACCESSION NUMBER:         2004:392315  HCAPLUS
DOCUMENT NUMBER:          140:400061
TITLE:                    Methods and therapeutic combinations using sterol
                          absorption inhibitor for the treatment of autoimmune
                          disorders
INVENTOR(S):              Erbey, John R.; Fine, Jay S.; Veltri, Enrico P.
PATENT ASSIGNEE(S):       Schering Corporation, USA
SOURCE:                   U.S. Pat. Appl. Publ., 31 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
     US 2004092499      A1   20040513      US 2003-700909   20031104
     WO 2004043456      A1   20040527      WO 2003-US35027  20031103
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR,
             HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA,
```

MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU,
ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

WO 2004043457 A1 20040527 WO 2003-US35058 20031104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR,
HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA,
MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU,
ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-424165P P 20021106
US 2003-493318P P 20030807

GI



I

AB The present invention provides methods for treating or preventing an autoimmune disorder and assocd. conditions by administering at least one sterol absorption inhibitor and compns., therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b) at least one autoimmune disorder treatment which can be useful for preventing or treating an autoimmune disorder and assocd. conditions. Prepn. of sterol absorption inhibitor compd. I is described.

L10 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:100508 HCAPLUS
DOCUMENT NUMBER: 140:157440
TITLE: Methods for treating an autoimmune disease using a soluble CTLA4 molecule in combination with a DMARD or NSAID
INVENTOR(S): Cohen, Robert; Carr, Suzette; Hagerty, David; Peach, Robert J.; Becker, Jean-Claude
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 189 pp., Cont.-in-part of U.S. Ser. No. 898,195.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004022787	A1	20040205	US 2003-419008	20030418
US 2003083246	A1	20030501	US 2001-898195	20010702

PRIORITY APPLN. INFO.: US 2000-215913P P 20000703
US 2001-898195 A2 20010702

AB The present invention relates to compns. and methods for treating immune system diseases such as rheumatic disease, by administering to a subject sol. CTLA4 (cytotoxic T lymphocyte antigen 4) mols. that block endogenous B7 (CD80) mols. from binding their ligands, alone, or in conjunction with other agents including disease modifying anti-rheumatic drugs (DMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs). The sol. CTLA4 mol. comprises the extracellular domain (residues 1-124) of full-length human CTLA4, which may be fused at the N-terminus with the signal peptide of oncostatin M and at the C-terminal end with an Igγ1 const. region. Single-site and double-site CTLA4 mutant sequences are also constructed, including L104E/A29Y-CTLA4/Ig, L104E/A29L-CTLA4/Ig, L104E/A29T-CTLA4/Ig, and L104E/A29W-CTLA4/Ig. CTLA4/Ig administered at 10 mg/kg (plus methotrexate) has superior efficacy in treatment of rheumatoid arthritis compared to placebo (plus methotrexate) based on efficacy parameters of the American Collage of Rheumatol. Core Data Set and Response Definitions (ACR). Binding kinetics to CD86 and CD80, pharmacokinetics, and pharmacodynamics of C-reactive protein, rheumatoid factor, interleukin-2 receptor, interleukin -6, and tumor necrosis factor α are provided.

```
=> d his

     (FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1             STRUCTURE UPLOADED
L2           3 S L1
L3          52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4           1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5           0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6          32 S COX-II () INHIBITOR?
L7        2445 S COX-2 () INHIBITOR?
L8        2447 S L7 OR L6 AND MYOSITIS?
L9        3199 S L7 OR MYOSITIS?
L10         15 S L7 AND MYOSITIS?
L11          0 S L10 AND REVIEW/DT

=> d l10, ibib abs, 1-15

L10  ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2004:392315 HCAPLUS
DOCUMENT NUMBER: 140:400061

TITLE: Methods and therapeutic combinations using sterol absorption inhibitor for the treatment of autoimmune disorders
INVENTOR(S): Erbey, John R.; Fine, Jay S.; Veltri, Enrico P.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092499	A1	20040513	US 2003-700909	20031104
WO 2004043456	A1	20040527	WO 2003-US35027	20031103

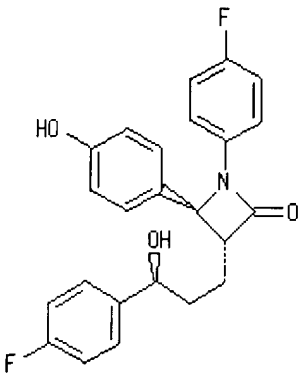
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2004043457	A1	20040527	WO 2003-US35058	20031104

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 2002-424165P	P	20021106
	US 2003-493318P	P	20030807

GI



I

AB The present invention provides methods for treating or preventing an autoimmune disorder and assocd. conditions by administering at least one sterol absorption inhibitor and compns., therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b)

at least one autoimmune disorder treatment which can be useful for preventing or treating an autoimmune disorder and assocd. conditions. Prepn. of sterol absorption inhibitor compd. I is described.

L10 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:100508 HCAPLUS
DOCUMENT NUMBER: 140:157440
TITLE: Methods for treating an autoimmune disease using a soluble CTLA4 molecule in combination with a DMARD or NSAID
INVENTOR(S): Cohen, Robert; Carr, Suzette; Hagerty, David; Peach, Robert J.; Becker, Jean-Claude
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 189 pp., Cont.-in-part of U.S. Ser. No. 898,195.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004022787	A1	20040205	US 2003-419008	20030418
US 2003083246	A1	20030501	US 2001-898195	20010702

PRIORITY APPLN. INFO.: US 2000-215913P P 20000703
US 2001-898195 A2 20010702

AB The present invention relates to compns. and methods for treating immune system diseases such as rheumatic disease, by administering to a subject sol. CTLA4 (cytotoxic T lymphocyte antigen 4) mols. that block endogenous B7 (CD80) mols. from binding their ligands, alone, or in conjunction with other agents including disease modifying anti-rheumatic drugs (DMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs). The sol. CTLA4 mol. comprises the extracellular domain (residues 1-124) of full-length human CTLA4, which may be fused at the N-terminus with the signal peptide of oncostatin M and at the C-terminal end with an Igγ1 const. region. Single-site and double-site CTLA4 mutant sequences are also constructed, including L104E/A29Y-CTLA4/Ig, L104E/A29L-CTLA4/Ig, L104E/A29T-CTLA4/Ig, and L104E/A29W-CTLA4/Ig. CTLA4/Ig administered at 10 mg/kg (plus methotrexate) has superior efficacy in treatment of rheumatoid arthritis compared to placebo (plus methotrexate) based on efficacy parameters of the American Collage of Rheumatol. Core Data Set and Response Definitions (ACR). Binding kinetics to CD86 and CD80, pharmacokinetics, and pharmacodynamics of C-reactive protein, rheumatoid factor, interleukin-2 receptor, interleukin -6, and tumor necrosis factor α are provided.

L10 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:855818 HCAPLUS
DOCUMENT NUMBER: 139:345914
TITLE: Treating an autoimmune disease using a soluble CTLA4 molecule in combination with a DMARD or NSAID drug
INVENTOR(S): Cohen, Robert; Carr, Suzette; Hagerty, David; Peach, Robert J.; Becker, Jean-Claude
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 339 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088991	A1	20031030	WO 2003-US12356	20030418
WO 2003088991	C2	20040205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-373852P P 20020419
US 2002-407246P P 20020830

AB The present invention relates to compns. and methods for treating immune system diseases such as rheumatic disease, by administering to a subject sol. CTLA4 mols. that block endogenous B7 mols. from binding their ligands, alone, or in conjunction with other agents including disease modifying anti-rheumatic drugs (DMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs). The sol. CTLA4 mol. comprises the extracellular domain (residues 1-124) of full-length human CTLA4, which may be fused at the N-terminus with the signal peptide of oncostatin M and at the C-terminal end with an Ig C γ1 domain. Single-site and double-site CTLA4 mutant sequences are also constructed, including L104E/A29Y-CTLA4/Ig, L104E/A29L-CTLA4/Ig, L104E/A29T-CTLA4/Ig, and L104E/A29W-CTLA4/Ig. CTLA4/Ig administered at 10 mg/kg (plus methotrexate) has superior efficacy in treatment of rheumatoid arthritis compared to placebo (plus metrotrexate) based on efficacy parameters of the American Collage of Rheumatol. Core Data Set and Response Definitions (ACR). Binding kinetics to CD86 and CD80, pharmacokinetics, and pharmacodynamics of C-reactive protein, rheumatoid factor, interleukin-2 receptor, interleukin -6, and tumor necrosis factor α are provided.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:356271 HCAPLUS
DOCUMENT NUMBER: 138:353983
TITLE: Preparation of 5-heterocyclo-1-(5-methanesulfonylpyridin-2-yl)-1H-pyrazoles as **COX-2 inhibitors**
INVENTOR(S): Sakya, Subas Man; Minich, Martha Lou
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037351	A1	20030508	WO 2002-IB3858	20020916
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1312367	A1	20030521	EP 2002-257242	20021018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002004429	A	20030916	BR 2002-4429	20021029
JP 2003183275	A2	20030703	JP 2002-319389	20021101
US 2003149026	A1	20030807	US 2002-285745	20021101

PRIORITY APPLN. INFO.: US 2001-335713P P 20011102
OTHER SOURCE(S): MARPAT 138:353983
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = II-VII (wherein m = 0-2; X = CR5, N); R1 = H, NO2, CN, etc.; R2 = H, NO2, CN, etc.; R3 = = satd. 3-4 membered heterocyclyl, (un)satd. or arom. 7-9 membered heterocyclyl; R4 = alkyl, fluoroalkyl; R5 = H, halo, OH, etc.], useful in the treatment or alleviation of inflammation and other inflammation assocd. disorders, such as arthritis, colon cancer, and Alzheimer's disease in mammals, preferably humans, dogs, cats and livestock animals, were prepd. E.g., prepn. of I [A = 5-methanesulfonylpyridin-2-yl; R1 = CN; R2 = CF3; R3 = azepan-1-yl], starting from 5-chloro-1-(5-methanesulfonylpyridin-2-yl)-3-trifluoromethyl-1H-pyrazole-4-carbonitrile, was described. Most compds. in examples showed IC50 values of 0.001 μM to 3 μM with respect to inhibition of COX-2 in either the canine or human assays.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:356256 HCAPLUS
DOCUMENT NUMBER: 138:353982
TITLE: Preparation of 1-(5-sulfonyl-pyridin-2-yl)-5-(methylidene-cycloalkylmethoxy)-1H-pyrazole-4-carbonitriles as cyclooxygenase inhibitors for the treating arthritis, neurodegeneration and colon cancer
INVENTOR(S): Sakya, Subas Man; Shavnya, Andrei
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037336	A1	20030508	WO 2002-IB3833	20020916
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
BR 2002004430	A	20030916	BR 2002-4430	20021029
JP 2003137884	A2	20030514	JP 2002-319649	20021101
US 2003134839	A1	20030717	US 2002-285746	20021101

PRIORITY APPLN. INFO.: US 2001-335736P P 20011102
OTHER SOURCE(S): MARPAT 138:353982
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = II-VIII (wherein m = 0-2; X = CR5, N); R1 = H, NO2, CN, etc.; R2 = H, NO2, CN, etc.; B = O, S, NR3; R3 = H, alkyl; R4 = NH2, mono- or dialkylamino, cycloalkylamino, etc.; R5 = H, halo, OH, etc.; G = 3-8 membered cycloalkyl or heterocycloalkyl; R6, R7 = H, alkyl, aryl, etc.], useful in the treatment or alleviation of inflammation and other inflammation assocd. disorders, such as arthritis, colon cancer, and Alzheimer's disease in mammals, preferably humans, dogs, cats and livestock animals, were prepd. Thus, reacting 5-chloro-1-(5-methanesulfonylpyridin-2-yl)-3-trifluoromethyl-1H-pyrazole-4-carbonitrile with (4-methylenecyclohexyl)methanol in the presence of KF in DMSO afforded IX. Most compds. in the examples showed IC50 of 0.001 μM to 3 μM with respect to inhibition of COX-2 in either the canine or human assays.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:356255 HCAPLUS
DOCUMENT NUMBER: 138:353981
TITLE: Preparation of heteroaryl substituted pyrazoles as selective **COX-2 inhibitors**
INVENTOR(S): Minich, Martha Lou; Demollo, Kristin Marie Lundy; Sakya, Subas Man; Shavnya, Andrei
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037335	A1	20030508	WO 2002-IB3818	20020916
WO 2003037335	C1	20030814		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003137883	A2	20030514	JP 2002-319566	20021101
US 2003134858	A1	20030717	US 2002-285744	20021101

PRIORITY APPLN. INFO.: US 2001-335733P P 20011102
OTHER SOURCE(S): MARPAT 138:353981
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = II-VIII (wherein m = 0-2; X = CR5, N); R1 = H, NO2, CN, etc.; R2 = H, NO2, CN, etc.; B = O, S, SO, SO2, NR6; R3 = alkyl, aryl, cycloalkyl, etc.; R4 = mono- or dialkylamino, cycloalkylamino, etc.; R5 = H, halo, OH, etc.; R6 = H, alkyl, aryl, etc.], useful in the treatment or alleviation of inflammation and other inflammation assocd. disorders, such as arthritis, colon cancer, and Alzheimer's disease in mammals, preferably humans, dogs, cats and livestock animals, were prepd. Thus, treating 6-[4-cyano-5-(2,2-dimethylpropylamino)-3-trifluoromethylpyrazol-1-yl]pyridine-3-sulfonamide with Ac2O in the presence of Et3N and DMAP in CH2Cl2 afforded 80% IX which was then converted into its Na salt. Most compds. prepd. in Examples showed IC50 of 0.001 μM to 3 μM with respect to inhibition of COX-2 in either the canine or human assays.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:356027 HCAPLUS
DOCUMENT NUMBER: 138:353980
TITLE: Preparation of 5-(alkylidene-cycloalkyl)- and 5-(alkylidene-heterocyclyl)-pyrazoles as **COX-2 inhibitors** for treating inflammation and other inflammation assocd. disorders
INVENTOR(S): Sakya, Subas Man; Shavnya, Andrei
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1308446	A1	20030507	EP 2002-257340	20021022

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: US 2001-335736 A 20011102
OTHER SOURCE(S): MARPAT 138:353980
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = II-VIII (wherein m = 0-2; X = CR5, N); R1 = H, NO2, CN, etc.; R2 = H, NO2, CN, etc.; B = O, S, NR3; R3 = H, alkyl; R4 = NH2, mono- or dialkylamino, cycloalkylamino, etc.; R5 = H, halo, OH, etc.; G = 3-8 membered cycloalkyl or heterocycloalkyl; R6, R7 = H, alkyl, aryl, etc.], useful in the treatment or alleviation of inflammation and other inflammation assocd. disorders, such as arthritis, colon cancer, and Alzheimer's disease in mammals, preferably humans, dogs, cats and livestock animals, were prepd. Thus, reacting 5-chloro-1-(5-methanesulfonylpyridin-2-yl)-3-trifluoromethyl-1H-pyrazole-4-carbonitrile with (4-methylenecyclohexyl)methanol in the presence of KF in DMSO afforded IX. Most compds. in the examples showed IC50 of 0.001 μM to 3 μM with respect to inhibition of COX-2 in either the canine or human assays.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:356026 HCAPLUS
DOCUMENT NUMBER: 138:353979
TITLE: Preparation of heteroaryl substituted pyrazoles as selective **COX-2 inhibitors**
INVENTOR(S): Demello, Kristin Marie Lundy; Minich, Martha Lou; Sakya, Subas Man; Shavnya, Andrei
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1308445	A1	20030507	EP 2002-257240	20021018

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: US 2001-335733 A 20011102
OTHER SOURCE(S): MARPAT 138:353979
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = II-VIII (wherein m = 0-2; X = CR5, N); R1 = H, NO2, CN, etc.; R2 = H, NO2, CN, etc.; B = O, S, SO, SO2, NR6; R3 = alkyl, aryl, cycloalkyl, etc.; R4 = mono- or dialkylamino, cycloalkylamino, etc.; R5 = H, halo, OH, etc.; R6 = H, alkyl, aryl, etc.], useful in the treatment or alleviation of inflammation and other inflammation assocd. disorders, such as arthritis, colon cancer, and Alzheimer's disease in mammals, preferably humans, dogs, cats and livestock animals, were prepd. Thus, treating 6-[4-cyano-5-(2,2-dimethylpropylamino)-3-trifluoromethylpyrazol-1-yl]pyridine-3-sulfonamide with Ac2O in the presence of Et3N and DMAP in CH2Cl2 afforded 80% IX which was then converted into its Na salt.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:927258 HCAPLUS
DOCUMENT NUMBER: 138:16609
TITLE: Skin-permeable selective cyclooxygenase-2 inhibitor composition
INVENTOR(S): Lu, Guang Wei; Ewing, Gary D.; Tyle, Praveen; Stoller, Brenda M.; Gokhale, Rajeev; Gadre, Ashwini
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096435	A2	20021205	WO 2002-US17067	20020530
WO 2002096435	A3	20030501		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003161867	A1	20030828	US 2002-158342	20020530
NZ 529797	A	20031219	NZ 2002-529797	20020530
EP 1404345	A2	20040407	EP 2002-774123	20020530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:

US 2001-294838P	P	20010531
US 2001-350756P	P	20011113
WO 2002-US17067	W	20020530

OTHER SOURCE(S): MARPAT 138:16609

AB A skin deliverable pharmaceutical compn. comprises at least 1 selective cyclooxygenase-2 (**COX-2**) **inhibitory** drug or prodrug thereof solubilized in a pharmaceutically acceptable carrier that contains a low mol. wt. monohydric alc., and exhibits a skin permeation rate of the

therapeutic agent at least equal to that exhibited by a ref. soln. of the therapeutic agent in 70% aq. ethanol. A method of effecting targeted delivery of a selective **COX-2 inhibitory** drug to a site of pain and/or inflammation in a subject comprises topically administering such a compn. to skin of the subject, preferably at a locus overlying or adjacent to the site of pain and/or inflammation. A method of effecting systemic treatment of a subject having a COX-2 mediated disorder comprises transdermally administering such a compn., preferably by contacting the compn. with an area of skin of the subject ≥400 cm^2. Thus, celecoxib was obsd. in 70% aq. EtOH and this soln. provided greater skin flux of the drug.

L10 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:217017 HCAPLUS
DOCUMENT NUMBER: 137:91637
TITLE: COX-1 and COX-2 expression in osteoid osteomas
AUTHOR(S): Mungo, David V.; Zhang, Xinping; O'Keefe, Regis J.; Rosier, Randy N.; Puzas, J. Edward; Schwarz, Edward M.
CORPORATE SOURCE: Department of Orthopaedics, Medical Center, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Orthopaedic Research (2002), 20(1), 159-162
CODEN: JOREDR; ISSN: 0736-0266
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteoid osteoma is a benign bone forming neoplasm that is characterized by its small size (less than 2 cm), self-limited growth, and the tendency to cause extensive reactive changes in the adjacent tissue. The lesion classically presents with severe pain at night that is dramatically relieved by NSAIDs. The tumor was shown to express very high levels of prostaglandins, particularly PGE2 and PGI2. The high local levels of these prostaglandins are presumed to be the cause of the intense pain seen in patients with this lesion. One generally accepted form of treatment is the prolonged use of NSAIDs. Since the cyclooxygenases are thought to be the source of these prostaglandins, and the central target of NSAIDs, we evaluated the expression of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) in osteoid osteoma tissues from patients following surgery. In the 12 specimens examd. we found that the tumor osteoblasts had strong immunohistochem. staining for COX-2, while the staining in the surrounding host osteoblasts in the reactive bone was scant. Significant COX-1 staining was also detected in both tumor and host osteoblasts. For comparison we examd. the COX expression in human fracture callus, fibrous dysplasia, osteoblastoma, osteofibrous dysplasia, and **myositis** ossificans. With the exception of fracture callus, very limited amts. of COX-2 could be detected in these tissues. Taken together, we conclude that the increased prodn. of prostaglandins by osteoid osteomas implicates that COX-2 is one of the mediators of this condition. These findings suggest that the newly selective **COX-2 inhibitors** could be used to more safely treat osteoid osteomas.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

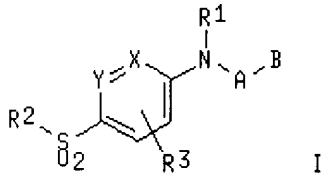
ACCESSION NUMBER: 2001:816621 HCAPLUS
DOCUMENT NUMBER: 135:357764
TITLE: Preparation of N-substituted para-

(sulfonyl)(hetero)arylamines as **COX-2 inhibitors**
INVENTOR(S): Krauss, Nancy Elisabeth; Mirzadegan, Taraneh; Smith, David Bernard; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083434	A2	20011108	WO 2001-EP4589	20010424
WO 2001083434	A3	20020328		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1278723	A2	20030129	EP 2001-943280	20010424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001010358	A	20030305	BR 2001-10358	20010424
JP 2003531886	T2	20031028	JP 2001-580863	20010424
US 2002052349	A1	20020502	US 2001-844061	20010426

PRIORITY APPLN. INFO.: US 2000-200310P P 20000428
WO 2001-EP4589 W 20010424

OTHER SOURCE(S): MARPAT 135:357764
GI



I

AB The title compds. [I; A = (CR2)n; n = 1-3; R = H, alkyl; B = (hetero)aryl; X, Y = CH, N; R1 = alkyl, alkenyl, aryl, etc.; R2 = alkyl, cycloalkyl, aryl, etc.; R3 = H, alkyl, halo, etc.] which have prostaglandin G/H synthase inhibitor activity and are suitable for the treatment of inflammatory diseases, such as **myositis**, synovitis, rheumatoid arthritis, osteoarthritis, gout, ankylosing spondylitis and bursitis, for the treatment of Alzheimer's disease or of an autoimmune disease such as systemic lupus erythematosus and type I diabetes, were prepd. and formulated. E.g., a multi-step synthesis of I [A = CH2; B = 4-MeC6H4; X, Y = CH; R1 = (CH2)2SO2Me; R2 = NH2; R3 = H] which showed IC50 of < 5.0 μM against COX-2, was given.

L10 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

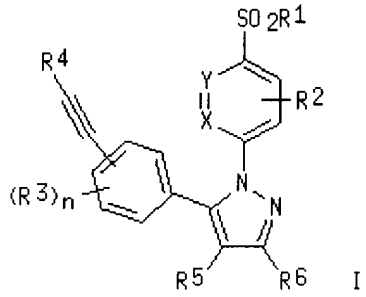
Full Text | Citing References

ACCESSION NUMBER: 2001:416498 HCAPLUS
DOCUMENT NUMBER: 135:19633

TITLE: Preparation of 5-alkynylphenyl-1-sulfonylarylpyrazoles as antiinflammatory and analgesic agents.
INVENTOR(S): Cheng, Hengmaio; Kawai, Akiyoshi
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1104758	A1	20010606	EP 2000-310533	20001128
EP 1104758	B1	20030723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6506779	B1	20030114	US 2000-723609	20001128
AT 245639	E	20030815	AT 2000-310533	20001128
PT 1104758	T	20031231	PT 2000-310533	20001128
ES 2200787	T3	20040316	ES 2000-310533	20001128
JP 2001206876	A2	20010731	JP 2000-367950	20001204
BR 2000006254	A	20011211	BR 2000-6254	20001204

PRIORITY APPLN. INFO.: US 1999-168698P P 19991203
OTHER SOURCE(S): MARPAT 135:19633
GI



I

AB Title compds. [I; n = 1, 2; X = CR7, N; Y = CR8, N; R1 = alkyl, NH2; R2 = H, halo, alkyl, alkenyl, alkynyl, alkoxy, alkylcarbonyl, CHO, cyano, NO2, CO2H, etc.; R3 = H, halo, alkyl, alkenyl, alkynyl, alkoxy, alkylcarbonyl, CHO, cyano, NO2, etc.; R4 = H, (substituted) aryl(alkyl), heteroaryl(alkyl); R5 = H, halo, alkyl, alkenyl, alkynyl, alkoxy, alkylcarbonyl, CHO, cyano, NO2, CO2H, alkoxycarbonyl, aminocarbonyl, etc.; R6 = H, halo, alkyl, alkenyl, alkynyl, alkoxy, alkylcarbonyl, CHO, cyano, NO2, CO2H, etc.; R7 = H, halo, OH, SH, alkyl, alkoxy, haloalkoxy, alkenyl, alkynyl, cyano, CHO, alkylcarbonyl, CO2H, alkoxycarbonyl, etc.], were prepd. Thus, 4,4,4-trifluoro-1-(4-bromophenyl)-1,3-butanedione and 2-hydrazino-5-methylsulfonylpyridine hydrochloride were refluxed together in EtOH for 3 days to give 5-methylsulfonyl-2-[5-(4-bromophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]pyridine. The latter was heated with CuI, Pd(PPh3)4, Et3N, and Me3SiC≡CH at 80° for 2 h to give a crude product which was stirred with K2CO3 in MeOH to give 5-methylsulfonyl-2-[5-(4-ethynylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]pyridine. I selectively inhibited cyclooxygenase-2 in canine whole blood ex vivo detns.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:12289 HCAPLUS
DOCUMENT NUMBER: 134:80816
TITLE: Combination of tumors necrosis factor (TNF) antagonists and cyclooxygenase 2 (**COX-2**) **inhibitors** for the treatment of inflammation
INVENTOR(S): Keane, J. Timothy
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000229	A1	20010104	WO 2000-US16292	20000626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1189628	A1	20020327	EP 2000-944668	20000626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003503360	T2	20030128	JP 2001-505937	20000626
NZ 515711	A	20040130	NZ 2000-515711	20000626
ZA 2001010349	A	20021218	ZA 2001-10349	20011218

PRIORITY APPLN. INFO.: US 1999-141238P P 19990624
WO 2000-US16292 W 20000626

OTHER SOURCE(S): MARPAT 134:80816
AB The invention provides combinations of a TNF antagonizing agent and a COX-2 inhibiting agent for treating inflammatory disease in a mammal.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:241195 HCAPLUS
DOCUMENT NUMBER: 132:265105
TITLE: Preparation of biphenylene lactams as prostaglandin receptor ligands
INVENTOR(S): Atkinson, Joseph G.; Lacombe, Patrick; Labelle, Marc; Ruel, Rejean
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

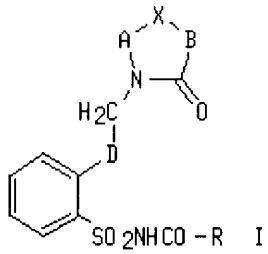
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020398	A1	20000413	WO 1999-CA927	19991005
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6277839	B1	20010821	US 1999-410583	19991001
CA 2346445	AA	20000413	CA 1999-2346445	19991005
AU 9959648	A1	20000426	AU 1999-59648	19991005
AU 752820	B2	20021003		
EP 1119555	A1	20010801	EP 1999-970085	19991005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526535	T2	20020820	JP 2000-574515	19991005

PRIORITY APPLN. INFO.: US 1998-103371P P 19981007
WO 1999-CA927 W 19991005

OTHER SOURCE(S): MARPAT 132:265105

GI



I

AB Compds. of general formula I [A, B = independently (un)substituted 2-benzenediyl or 2-heteroarylenediyl; X = CH2CH2, CH:CH, CH2Y, YCH2, CH2CH2CH2, etc, where Y = O, S, CF2, or CO; D = (un)substituted benzendiyl; R = C1-6alkyl, (CR1R2)nO-Ph, (CR1R2)nO-heteroaryl, O-(CR1R2)nPh, etc, a proviso is given] are prepd. No biol. data is given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

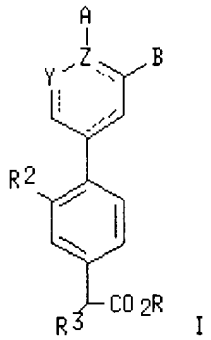
ACCESSION NUMBER: 1999:529121 HCAPLUS
DOCUMENT NUMBER: 131:157648
TITLE: Preparation of biarylacetic acid derivatives as **COX-2 inhibitors**
INVENTOR(S): Bayly, Christopher I.; Black, Cameron; Ouimet, Nathalie; Percival, David; Leger, Serge; Ouellet, Marc
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941224	A1	19990819	WO 1999-CA120	19990211
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5994379	A	19991130	US 1999-246925	19990209
CA 2318966	AA	19990819	CA 1999-2318966	19990211
AU 9925065	A1	19990830	AU 1999-25065	19990211
AU 749618	B2	20020627		
EP 1054857	A1	20001129	EP 1999-904652	19990211
EP 1054857	B1	20031105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002503647	T2	20020205	JP 2000-531421	19990211
AT 253545	E	20031115	AT 1999-904652	19990211

PRIORITY APPLN. INFO.: US 1998-74627P P 19980213
WO 1999-CA120 W 19990211

OTHER SOURCE(S): MARPAT 131:157648
GI



I

AB Title compds. [I; R = H, CH3; R2 = H, F; R3 = H, CH3; Y = C(OEt), C(OMe), N, CH, C:O; Z = C, N; A = H; B = OEt, SEt, OPr, (E)-CH:CHCH3, CH3; A-B = NHC(CH3):CH; CHN(CH3)CH, OC(CH3):CH, SC(CH3):CH, NHC(CH3):N, N:C(CH3)O, N:C(CH3)S, OC(CH3):N, SC(CH3):N, CH2N(CH3)CH, CHC(CH3)N:CH; dotted bond = single, double in relation to Y, Z, A, B], pharmaceutically acceptable salts (sodium, potassium, calcium, magnesium), tautomer, and esters thereof are prepd. and compns. which contain such compds. and methods of use the compds. are presented and tested as inhibitors of COX-2. Thus, the title compd. I (Y = C(OEt); Z = C; A = H; B = OEt; R = H; R2 = H; R3 = CH3; dotted bonds = double bonds) was prepd. from 3,5-diethoxyphenol in 3 steps.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d hi
L11 HAS NO ANSWERS
L7          2445 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COX-2 (W) INHIBITOR?
L10           15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND MYOSITIS?
L11            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND REVIEW/DT


=> d his

     (FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1               STRUCTURE UPLOADED
L2             3 S L1
L3            52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4             1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5             0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6            32 S COX-II () INHIBITOR?
L7          2445 S COX-2 () INHIBITOR?
L8          2447 S L7 OR L6 AND MYOSITIS?
L9          3199 S L7 OR MYOSITIS?
L10           15 S L7 AND MYOSITIS?
L11            0 S L10 AND REVIEW/DT

=> s l6 and myositis?
            769 MYOSITIS?
L12           2 L6 AND MYOSITIS?

=> s l12 and review/dt
       1738344 REVIEW/DT
L13            0 L12 AND REVIEW/DT

=> d his

     (FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1               STRUCTURE UPLOADED
L2             3 S L1
L3            52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4             1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5             0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6            32 S COX-II () INHIBITOR?
L7          2445 S COX-2 () INHIBITOR?
L8          2447 S L7 OR L6 AND MYOSITIS?
L9          3199 S L7 OR MYOSITIS?
L10           15 S L7 AND MYOSITIS?
```

```
L11             0 S L10 AND REVIEW/DT
L12             2 S L6 AND MYOSITIS?
L13             0 S L12 AND REVIEW/DT

=> s l6 and synovitis?
           1146 SYNOVITIS?
L14           2 L6 AND SYNOVITIS?

=> s l14 and review/dt
         1738344 REVIEW/DT
L15             0 L14 AND REVIEW/DT

=> s l7 and synovitis?
           1146 SYNOVITIS?
L16          15 L7 AND SYNOVITIS?

=> s l16 and review/dt
         1738344 REVIEW/DT
L17             3 L16 AND REVIEW/DT

=> d l17, ibib abs, 1-3

L17  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2002:857962 HCAPLUS
DOCUMENT NUMBER: 138:135283
TITLE: The role of cyclooxygenases and prostaglandins in the pathogenesis of rheumatoid arthritis
AUTHOR(S): Stanczyk, Joanna; Kowalski, Marek Leszek
CORPORATE SOURCE: Katedra Immunol. i Zakl. Immunol. Klin., Akad. Med., Lodz, 92-213, Pol.
SOURCE: Polski Merkuriusz Lekarski (2001), 11(65), 438-443
CODEN: PMLOB9; ISSN: 1426-9686
PUBLISHER: Medpress
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Polish

AB A review. Rheumatoid arthritis (RA) is a systemic inflammatory disease with polyarticularsynovitis leading to formation of rheumatoid pannus and subsequent erosion of articular cartilage and bone. Prostaglandins (PGs) - a group of arachidonic acid metabolites found at elevated levels in synovial fluid and synovial membrane are considered to play a pivotal role in development of vasodilatation, fluid extravasation and pain in synovial tissues. Moreover, there is increasing evidence that PGs (esp. prostaglandin E2) are mediators involved in complex interactions leading to development of erosions of articular cartilage and juxta-articular bone. Cyclooxygenase is an enzyme playing crucial role in PG prodn. It is known that two forms of cyclooxygenase exist: cyclooxygenase-1 (COX-1) playing house-keeping functions and cyclooxygenase-2 (COX-2) involved in inflammatory responses. Synovial tissues from patients with RA are shown to contain COX-2 and to a less extent COX-1. COX-2 expression in rheumatoid synovium is induced by proinflammatory cytokines, mainly IL-1, while corticosteroids are capable of inhibiting COX-2 expression. The understanding of crucial role of COX-2 in synovial inflammation led to development of new group of anti-inflammatory agents - selective **COX-2 inhibitors**, that inhibit specifically COX-2, providing effective anti-inflammatory action without the side effects assocd. with inhibition of COX-1. In the context of widespread use of selective **COX-2 inhibitors** hypothetical role of COX-1 in RA pathol. should be elucidated.

L17 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:292839 HCAPLUS
DOCUMENT NUMBER: 129:80257
TITLE: Expression and regulation of COX-2 in synovial tissues of arthritic patients
AUTHOR(S): Crofford, L. J.
CORPORATE SOURCE: Department of Internal Medicine, Division of Rheumatology, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Improved Non-Steroid Anti-Inflammatory Drugs: COX-2 Enzyme Inhibitors, Proceedings of a Conference, London, Oct. 10-11, 1995 (1996), Meeting Date 1995, 133-143. Editor(s): Vane, John R.; Botting, Jack H.; Botting, Regina M. Kluwer: Dordrecht, Neth.
CODEN: 65ZRAF
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review, with 44 refs. Available data regarding expression and regulation of cyclooxygenase (COX)-2 in synovial tissue is summarized. The pot. importance of a highly regulated enzyme in the prostaglandin synthetic pathway for rapid and highly localized prodn. of prostaglandins is discussed. Finally, the author speculates on the role of COX-2 in the pathogenesis of inflammatory **synovitis** and the pot. for specific **COX-2 inhibitors** as treatments for chronic inflammatory arthritis.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:645437 HCAPLUS
DOCUMENT NUMBER: 127:305964
TITLE: Expression and regulation of cyclooxygenase-2 in synovial tissues of arthritic patients
AUTHOR(S): Crofford, L. J.
CORPORATE SOURCE: Department of Internal Medicine, University of Michigan, Ann Arbor, MI, 48109-0531, USA
SOURCE: New Targets in Inflammation: Inhibitors of COX-2 or Adhesion Molecules, Proceedings of a Conference, New Orleans, Apr. 15-16, 1996 (1996), 83-91. Editor(s): Bazan, Nicolas G.; Botting, Jack H.; Vane, John R. Kluwer: Dordrecht, Neth.
CODEN: 65DFA5
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review, with 30 refs. The available data regarding expression and regulation of COX-2 in synovial tissues are summarized. The role of COX-2 in the pathogenesis of the inflammatory **synovitis** of rheumatoid arthritis and the potential for **COX-2 inhibitors** in the treatment of chronic inflammatory arthritis are discussed.

=> d his

(FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1 STRUCTURE UPLOADED

```
L2              3 S L1
L3             52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4              1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5              0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6             32 S COX-II () INHIBITOR?
L7           2445 S COX-2 () INHIBITOR?
L8           2447 S L7 OR L6 AND MYOSITIS?
L9           3199 S L7 OR MYOSITIS?
L10            15 S L7 AND MYOSITIS?
L11             0 S L10 AND REVIEW/DT
L12             2 S L6 AND MYOSITIS?
L13             0 S L12 AND REVIEW/DT
L14             2 S L6 AND SYNOVITIS?
L15             0 S L14 AND REVIEW/DT
L16            15 S L7 AND SYNOVITIS?
L17             3 S L16 AND REVIEW/DT

=> s l7 and arthritis?
         32941 ARTHRITIS?
L18        291 L7 AND ARTHRITIS?

=> s l18 and review/dt
       1738344 REVIEW/DT
L19        100 L18 AND REVIEW/DT

=> d l19, ibib abs, 1-5

L19  ANSWER 1 OF 100  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2004:238500  HCAPLUS
DOCUMENT NUMBER:          140:367916
TITLE:                    Cyclooxygenase-2 inhibitors in lung cancer
AUTHOR(S):                Ramalingam, Sakkaraiappan; Belani, Chandra P.
CORPORATE SOURCE:         Division of Hematology/Oncology, Lung and Thoracic
                          Cancer Program, University of Pittsburgh Cancer
                          Institute, University of Pittsburgh School of
                          Medicine, PA, USA
SOURCE:                   Clinical Lung Cancer (2004), 5(4), 245-253
                          CODEN: CLCLCA; ISSN: 1525-7304
PUBLISHER:                Cancer Information Group
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
```

AB A review. Prostanoids produced by the arachidonic acid pathway play an important role in multiple stages of carcinogenesis and progression of cancer. Cyclooxygenase (COX), which exists in 2 isoforms, is the rate-limiting enzyme in the COX pathway. Cyclooxygenase-1 is constitutively expressed in normal tissues and is essential for several important physiol. functions. Cyclooxygenase-2 is selectively overexpressed in neoplastic and inflammatory tissues. Non-small-cell lung cancer (NSCLC), esp. adenocarcinomas, overexpress COX-2, which contributes to the progression of malignancy by several mechanisms. This represents the basis of therapy with **COX-2 inhibitors**. Cyclooxygenase-2 inhibitors, which are currently in clin. use for the management of

inflammatory **arthritis**, are well tolerated by patients. They exhibit anticancer activity by several mechanisms including induction of apoptosis, inhibition of angiogenesis, and decreased invasiveness and metastatic potential. These effects have been documented in several preclin. studies. Clin. efficacy of **COX-2 inhibitors** in the treatment of NSCLC is presently undergoing evaluation.

REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 100 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:197787 HCAPLUS
DOCUMENT NUMBER: 140:192019
TITLE: Clinical pharmacology of novel selective **COX-2 inhibitors**
AUTHOR(S): Tacconelli, S.; Capone, M. L.; Patrignani, P.
CORPORATE SOURCE: Department of Medicine and Center of Excellence on Aging, School of Medicine, "G. d'Annunzio" University, Chieti, 66013, Italy
SOURCE: Current Pharmaceutical Design (2004), 10(6), 589-601
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Novel coxibs (i.e. etoricoxib, valdecoxib, parecoxib and lumiracoxib) with enhanced biochem. cyclooxygenase (COX)-2 selectivity over that of rofecoxib and celecoxib have been recently developed. They have the potential advantage to spare COX-1 activity, thus reducing gastrointestinal toxicity, even when administered at high doses to improve efficacy. They are characterized by different pharmacodynamic and pharmacokinetics features. The higher biochem. selectivity of valdecoxib than celecoxib, evidenced in vitro, may be clin. relevant leading to an improved gastrointestinal safety. Interestingly, parecoxib, a pro-drug of valdecoxib, is the only injectable coxib. Etoricoxib shows only a slightly improved COX-2 selectivity than rofecoxib, a highly selective **COX-2 inhibitor** that has been reported to halve the incidence of serious gastrointestinal toxicity compared to nonselective nonsteroidal antiinflammatory drugs (NSAIDs). Lumiracoxib, the most selective **COX-2 inhibitor** in vitro, is the only acidic coxib. The hypothesis that this chem. property may lead to an increased and persistent drug accumulation in inflammatory sites and consequently to an improved clin. efficacy, however, remains to be verified. Several randomized clin. studies suggest that the novel coxibs have comparable efficacy to nonselective NSAIDs in the treatment of osteoarthritis, rheumatoid **arthritis** and acute pain, but they share similar renal side-effects. The apparent dose-dependence of renal toxicity may limit the use of higher doses of the novel coxibs for improved efficacy. Large-size randomized clin. trials are ongoing to define the gastrointestinal and cardiovascular safety of the novel coxibs.

REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 100 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:21699 HCAPLUS
DOCUMENT NUMBER: 140:104298
TITLE: Targeting cyclooxygenase-2 in human neoplasia:

Rationale and promise
AUTHOR(S): Dannenberg, Andrew J.; Subbaramaiah, Kotha
CORPORATE SOURCE: Department of Medicine, Weill Medical College of Cornell University and Strang Cancer Prevention Center, New York, NY, 10021, USA
SOURCE: Cancer Cell (2003), 4(6), 431-436
CODEN: CCAECI; ISSN: 1535-6108
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Several lines of evidence suggest that cyclooxygenase-2 (COX-2) is a rational target for anticancer therapy. Selective **COX-2 inhibitors** have been used extensively to treat patients with **arthritis** and possess and excellent safety profile. Based on these findings, numerous clin. trials are under way to investigate the potential efficacy of selective **COX-2 inhibitors** in the prevention and treatment of a variety of cancers. Here we focus on the rationale for targeting COX-2 as a strategy to prevent or treat human malignancies.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 100 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2004:21595 HCAPLUS
DOCUMENT NUMBER: 140:70138
TITLE: COX-2-specific inhibitors: celecoxib and second-generation agents
AUTHOR(S): Bensen, William G.
CORPORATE SOURCE: St. Joseph's Hospital, McMaster University, Hamilton, ON, Can.
SOURCE: Pain (2003), 515-521. Editor(s): Bountra, Chas; Munglani, Rajesh; Schmidt, William K. Marcel Dekker, Inc.: New York, N. Y.
CODEN: 69EYYH; ISBN: 0-8247-8865-6
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review. The discovery of COX-2 specific inhibitors that appear to relieve pain and inflammation with less risk of toxicity than nonspecific COX-1/**COX-2 inhibitors** represents a major advance in antiinflammatory and analgesic therapy. Celecoxib appears to be both safe and effective for the treatment of the signs and symptoms of osteoarthritis and rheumatoid **arthritis**. In clin. trials, celecoxib was assocd. with a markedly lower rate of gastroduodenal injury than seen typically with NSAIDs, and also appears to possess little or no antiplatelet effect. Incidences of most adverse events, including gastrointestinal bleeding, and withdrawal rates because of adverse events with celecoxib were similar to placebo. Its COX-2-specific inhibitory properties thus introduce the possibility of effective relief of arthritic and other types of pain and inflammation with less risk of the COX-1-dependent toxicity obsd. with NSAIDs.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 100 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2004:8905 HCAPLUS
DOCUMENT NUMBER: 140:52605
TITLE: Lumiracoxib: a **COX-2 inhibitor** for the treatment

of **arthritis** and acute pain
AUTHOR(S): Feret, Brett
CORPORATE SOURCE: University of Rhode Island College of Pharmacy in Kingston, RI, USA
SOURCE: Formulary (2003), 38(9), 529, 531-534, 537
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Lumiracoxib (Prexige, Novartis) appears to be the next COX-2 specific inhibitor that will be marketed in the United States. Currently, lumiracoxib is being studied for the treatment of osteoarthritis, rheumatoid **arthritis**, and acute pain. Lumiracoxib has been shown in vitro to be more selective for the COX-2 isoenzyme compared to rofecoxib and celecoxib, but clin. head-to-head studies between these agents are lacking. Small controlled trials, presented in abstr. form, have shown lumiracoxib to have comparable efficacy to diclofenac and celecoxib in osteoarthritis. It has an adverse effect profile similar to other **COX-2 inhibitors** and superior to traditional NSAIDs concerning gastrointestinal safety, but cardiovascular and renal safety data are still not available. While existing clin. data on lumiracoxib are minimal and only published in abstr. form, research is ongoing, including comparing lumiracoxib to ibuprofen and naproxen in the largest **arthritis** trial undertaken to date. When the results of this study are published, lumiracoxib's efficacy and safety profile will be better understood.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1 STRUCTURE UPLOADED
L2 3 S L1
L3 52 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4 1 S L3

FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5 0 S L3

FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6 32 S COX-II () INHIBITOR?
L7 2445 S COX-2 () INHIBITOR?
L8 2447 S L7 OR L6 AND MYOSITIS?
L9 3199 S L7 OR MYOSITIS?
L10 15 S L7 AND MYOSITIS?
L11 0 S L10 AND REVIEW/DT
L12 2 S L6 AND MYOSITIS?
L13 0 S L12 AND REVIEW/DT
L14 2 S L6 AND SYNOVITIS?
L15 0 S L14 AND REVIEW/DT
L16 15 S L7 AND SYNOVITIS?
L17 3 S L16 AND REVIEW/DT
L18 291 S L7 AND ARTHRITIS?
L19 100 S L18 AND REVIEW/DT

```
=> s l7 and rheumatoid () arthrit?
         22837 RHEUMATOID
            11 RHEUMATOIDS
         22841 RHEUMATOID
                 (RHEUMATOID OR RHEUMATOIDS)
         33893 ARTHRIT?
         19746 RHEUMATOID (W) ARTHRIT?
L20        198 L7 AND RHEUMATOID (W) ARTHRIT?

=> s l20 and review/dt
       1738344 REVIEW/DT
L21         79 L20 AND REVIEW/DT

=> d l21, ibib abs, 1-5

L21  ANSWER 1 OF 79  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2004:197787 HCAPLUS
DOCUMENT NUMBER: 140:192019
TITLE: Clinical pharmacology of novel selective **COX-2 inhibitors**
AUTHOR(S): Tacconelli, S.; Capone, M. L.; Patrignani, P.
CORPORATE SOURCE: Department of Medicine and Center of Excellence on Aging, School of Medicine, "G. d'Annunzio" University, Chieti, 66013, Italy
SOURCE: Current Pharmaceutical Design (2004), 10(6), 589-601
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Novel coxibs (i.e. etoricoxib, valdecoxib, parecoxib and lumiracoxib) with enhanced biochem. cyclooxygenase (COX)-2 selectivity over that of rofecoxib and celecoxib have been recently developed. They have the potential advantage to spare COX-1 activity, thus reducing gastrointestinal toxicity, even when administered at high doses to improve efficacy. They are characterized by different pharmacodynamic and pharmacokinetics features. The higher biochem. selectivity of valdecoxib than celecoxib, evidenced in vitro, may be clin. relevant leading to an improved gastrointestinal safety. Interestingly, parecoxib, a pro-drug of valdecoxib, is the only injectable coxib. Etoricoxib shows only a slightly improved COX-2 selectivity than rofecoxib, a highly selective **COX-2 inhibitor** that has been reported to halve the incidence of serious gastrointestinal toxicity compared to nonselective nonsteroidal antiinflammatory drugs (NSAIDs). Lumiracoxib, the most selective **COX-2 inhibitor** in vitro, is the only acidic coxib. The hypothesis that this chem. property may lead to an increased and persistent drug accumulation in inflammatory sites and consequently to an improved clin. efficacy, however, remains to be verified. Several randomized clin. studies suggest that the novel coxibs have comparable efficacy to nonselective NSAIDs in the treatment of osteoarthritis, **rheumatoid arthritis** and acute pain, but they share similar renal side-effects. The apparent dose-dependence of renal toxicity may limit the use of higher doses of the novel coxibs for improved efficacy. Large-size randomized clin. trials are ongoing to define the gastrointestinal and cardiovascular safety of the novel coxibs.

REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 79 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:21595 HCAPLUS
DOCUMENT NUMBER: 140:70138
TITLE: COX-2-specific inhibitors: celecoxib and second-generation agents
AUTHOR(S): Bensen, William G.
CORPORATE SOURCE: St. Joseph's Hospital, McMaster University, Hamilton, ON, Can.
SOURCE: Pain (2003), 515-521. Editor(s): Bountra, Chas; Munglani, Rajesh; Schmidt, William K. Marcel Dekker, Inc.: New York, N. Y.
CODEN: 69EYYH; ISBN: 0-8247-8865-6
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review. The discovery of COX-2 specific inhibitors that appear to relieve pain and inflammation with less risk of toxicity than nonspecific COX-1/**COX-2 inhibitors** represents a major advance in antiinflammatory and analgesic therapy. Celecoxib appears to be both safe and effective for the treatment of the signs and symptoms of osteoarthritis and **rheumatoid arthritis**. In clin. trials, celecoxib was assocd. with a markedly lower rate of gastroduodenal injury than seen typically with NSAIDs, and also appears to possess little or no antiplatelet effect. Incidences of most adverse events, including gastrointestinal bleeding, and withdrawal rates because of adverse events with celecoxib were similar to placebo. Its COX-2-specific inhibitory properties thus introduce the possibility of effective relief of arthritic and other types of pain and inflammation with less risk of the COX-1-dependent toxicity obsd. with NSAIDs.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:8905 HCAPLUS
DOCUMENT NUMBER: 140:52605
TITLE: Lumiracoxib: a **COX-2 inhibitor** for the treatment of arthritis and acute pain
AUTHOR(S): Feret, Brett
CORPORATE SOURCE: University of Rhode Island College of Pharmacy in Kingston, RI, USA
SOURCE: Formulary (2003), 38(9), 529, 531-534, 537
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Lumiracoxib (Prexige, Novartis) appears to be the next COX-2 specific inhibitor that will be marketed in the United States. Currently, lumiracoxib is being studied for the treatment of osteoarthritis, **rheumatoid arthritis**, and acute pain. Lumiracoxib has been shown in vitro to be more selective for the COX-2 isoenzyme compared to rofecoxib and celecoxib, but clin. head-to-head studies between these agents are lacking. Small controlled trials, presented in abstr. form, have shown lumiracoxib to have comparable efficacy to diclofenac and celecoxib in osteoarthritis. It has an adverse effect profile similar to other **COX-2 inhibitors** and superior to traditional NSAIDs concerning gastrointestinal safety, but cardiovascular and renal safety data are still not available. While existing clin. data on lumiracoxib are minimal

and only published in abstr. form, research is ongoing, including comparing lumiracoxib to ibuprofen and naproxen in the largest arthritis trial undertaken to date. When the results of this study are published, lumiracoxib's efficacy and safety profile will be better understood.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 79 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:969629 HCAPLUS
DOCUMENT NUMBER: 140:12341
TITLE: Clinical pharmacology of selective **COX-2 inhibitors**
AUTHOR(S): Capone, M. L.; Tacconelli, S.; Sciulli, M. G.; Patrignani, P.
CORPORATE SOURCE: Department of Medicine and Center of Excellence on Aging, Ce.S.i. "G. d'Annunzio" University, Chieti, 66013, Italy
SOURCE: International Journal of Immunopathology and Pharmacology (2003), 16(2, Suppl.), 49-58
CODEN: IJIPE4; ISSN: 0394-6320
PUBLISHER: Biolife s.a.s.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The discovery of cyclooxygenase (COX)-2 has provided the rationale for the development of a new class of nonsteroidal antiinflammatory drugs (NSAIDs), the selective **COX-2 inhibitors** (denominated coxibs), with the aim of reducing the gastrointestinal (GI) toxicity assocd. with the administration of NSAIDs by virtue of COX-1 sparing. Rofecoxib and celecoxib are the first selective **COX-2 inhibitors** approved by the FDA and EMEA for the treatment of **rheumatoid arthritis** (RA), osteoarthritis (OA) and for relief of acute pain. Rofecoxib has been shown to spare COX-1 activity ex vivo, in platelets and gastric mucosa, when administered at therapeutic doses or above. In a large clin. trial, rofecoxib has been demonstrated to halve the incidence of serious upper GI events vs. a nonselective NSAID. Recently, other selective **COX-2 inhibitors** with different COX-1/COX-2 selectivity and pharmacokinetic features have been developed, i.e. valdecoxib, parecoxib, etoricoxib and lumiracoxib. The improved biochem. selectivity of valdecoxib vs. celecoxib in vitro (COX-1/COX-2 ratio: 60 vs. 30, resp.) may be clin. relevant leading to an improved GI safety. Interestingly, parecoxib, a pro-drug of valdecoxib, is the only injectable coxib. Etoricoxib, showing only a slightly higher COX-2 selectivity than rofecoxib in vitro (COX-1/COX-2 ratio: 344 vs. 272, resp.), has been reported to cause a similar specific COX-2 inhibition ex vivo that should translate into comparable GI safety. Lumiracoxib, the most selective **COX-2 inhibitor** in vitro (COX-1/COX-2 ratio: 400), is the only acidic coxib. It has been hypothesized that this peculiar chem. feature may lead to an enhanced concn. in inflammatory sites that may translate into an improved clin. efficacy. The results of clin. trials have shown that coxibs have a comparable clin. efficacy and renal toxicity and an improved GI safety vs. nonselective NSAIDs. Whether the different pharmacodynamic and pharmacokinetics features of the various coxibs will produce detectable differences in efficacy and toxicity remains to be evaluated in appropriate comparative randomized clin. studies.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 79 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:969623 HCAPLUS
DOCUMENT NUMBER: 140:399057
TITLE: The prospective use of **COX-2 inhibitors** for the treatment of temporomandibular joint inflammatory disorders
AUTHOR(S): Kerins, C. A.; Spears, R.; Bellinger, L. L.; Hutchins, B.
CORPORATE SOURCE: Department of Biomedical Sciences, Texas A and M University System Health Science Center, Baylor College of Dentistry, Dallas, TX, 75246, USA
SOURCE: International Journal of Immunopathology and Pharmacology (2003), 16(2, Suppl.), 1-9
CODEN: IJIPE4; ISSN: 0394-6320
PUBLISHER: Biolife s.a.s.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Development of a new class of drugs designed to selectively inhibit the inducible cyclooxygenase isoenzyme, COX-2, was initially prescribed for individuals diagnosed with osteoarthritis or **rheumatoid arthritis**. Although these inflammatory disorders are more typically related to the joints of the knee, ankle, or hand, the temporomandibular joint (TMJ) plays a special role due to its involvement in our normal day-to-day activities of eating and communicating. The TMJ, unlike most of the other joints, contains some unique morphol. characteristics that support various inflammatory disorders. An overview of these characteristics and the prospective use of the **COX-2 inhibitors** for temporomandibular joint inflammation are presented.

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d his

     (FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1             STRUCTURE UPLOADED
L2           3 S L1
L3          52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4           1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5           0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6          32 S COX-II () INHIBITOR?
L7        2445 S COX-2 () INHIBITOR?
L8        2447 S L7 OR L6 AND MYOSITIS?
L9        3199 S L7 OR MYOSITIS?
L10         15 S L7 AND MYOSITIS?
L11          0 S L10 AND REVIEW/DT
L12          2 S L6 AND MYOSITIS?
L13          0 S L12 AND REVIEW/DT
L14          2 S L6 AND SYNOVITIS?
L15          0 S L14 AND REVIEW/DT
L16         15 S L7 AND SYNOVITIS?
```

```
L17           3 S L16 AND REVIEW/DT
L18         291 S L7 AND ARTHRITIS?
L19         100 S L18 AND REVIEW/DT
L20         198 S L7 AND RHEUMATOID () ARTHRIT?
L21          79 S L20 AND REVIEW/DT

=> s l6 and rheumatoid () arthrit?
         22837 RHEUMATOID
            11 RHEUMATOIDS
         22841 RHEUMATOID
                 (RHEUMATOID OR RHEUMATOIDS)
         33893 ARTHRIT?
         19746 RHEUMATOID (W) ARTHRIT?
L22          2 L6 AND RHEUMATOID (W) ARTHRIT?

=> s l22 and review/dt
       1738344 REVIEW/DT
L23          0 L22 AND REVIEW/DT

=> s l6 and gout
          2856 GOUT
             3 GOUTS
          2859 GOUT
                 (GOUT OR GOUTS)
L24          2 L6 AND GOUT

=> s l24 and review/dt
       1738344 REVIEW/DT
L25          0 L24 AND REVIEW/DT

=> s l7 and gout
          2856 GOUT
             3 GOUTS
          2859 GOUT
                 (GOUT OR GOUTS)
L26         31 L7 AND GOUT

=> s l26 and review/dt
       1738344 REVIEW/DT
L27          2 L26 AND REVIEW/DT

=> d l27, ibib abs, 1-2

L27  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2003:875716 HCAPLUS
DOCUMENT NUMBER: 140:35188
TITLE: Clinical pharmacology of etoricoxib: a novel selective **COX-2 inhibitor**. [Erratum to document cited in CA139:300962]
AUTHOR(S): Patrignani, Paola; Capone, Marta L.; Tacconelli, Stefania
CORPORATE SOURCE: Div. Pharmacol., Dep. Med. Cent. Excellence on Aging, 'G. D'Ammunzio' Univ. Sch. Med., Chieti, 66013, Italy
SOURCE: Expert Opinion on Pharmacotherapy (2003), 4(3), 419
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The data points in Figure 8 were not assigned correctly; the cor. figure is given.

L27 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:149665 HCAPLUS
DOCUMENT NUMBER: 139:300962
TITLE: Clinical pharmacology of etoricoxib: a novel selective **COX-2 inhibitor**
AUTHOR(S): Patrignani, Paola; Capone, Marta L.; Tacconelli, Stefania
CORPORATE SOURCE: Div. Pharmacol., Dep. Med. Cent. Excellence on Aging, 'G. D'Ammunzio' Univ. Sch. Med., Chieti, 66013, Italy
SOURCE: Expert Opinion on Pharmacotherapy (2003), 4(2), 265-284
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with refs. The development of **COX-2 inhibitors** with improved biochem. selectivity (such as etoricoxib and valdecoxib) over that of com. available coxibs has been driven by the potential advantage of safety using higher coxib doses for increased efficacy. Etoricoxib has been approved in the UK as a once-daily medicine for symptomatic relief in the treatment of osteoarthritis (OA), rheumatoid arthritis (RA) and acute gouty arthritis. It is currently approved with addnl. indications (i.e., for relief of acute pain assocd. with dental surgery, for primary dysmenorrhea and for chronic musculo-skeletal pain, including chronic lower-back pain) in Mexico, Brazil and Peru. Etoricoxib has an in vitro COX-1/COX-2 IC50 ratio of 344, the highest of any coxib. The administration of therapeutic doses of etoricoxib to healthy subjects does not affect COX1 activity in circulating platelets and gastric biopsies. The profound inhibition of monocyte COX2 activity at 24 h after dosing, as predicted by a pharmacol. half-life of ~ 22 h, supports a once-daily dosing regimen of etoricoxib. In randomized, well-controlled clin. trials, etoricoxib has been shown to have a comparable clin. efficacy with traditional NSAIDs. Combined anal. of efficacy trials with etoricoxib vs. non-selective NSAIDs has shown that the drug halves both investigator-reported upper gastrointestinal perforation, ulcers and bleeds (PUBs) and confirmed PUBs, and reduces the need for gastroprotective agents and gastrointestinal comedications by ~ 40%. The risk of lower extremity edema and hypertension adverse experiences with etoricoxib was low and generally similar to comparator NSAIDs in a combined anal. of eight Phase III studies in OA, RA, chronic low-back pain and surveillance endoscopy. Large, randomised clin. trials have been planned to confirm the renal, gastrointestinal and cardiovascular safety of etoricoxib.
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)

FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1 STRUCTURE UPLOADED
L2 3 S L1
L3 52 S L1 FULL

```
     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4             1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5             0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6            32 S COX-II () INHIBITOR?
L7          2445 S COX-2 () INHIBITOR?
L8          2447 S L7 OR L6 AND MYOSITIS?
L9          3199 S L7 OR MYOSITIS?
L10           15 S L7 AND MYOSITIS?
L11            0 S L10 AND REVIEW/DT
L12            2 S L6 AND MYOSITIS?
L13            0 S L12 AND REVIEW/DT
L14            2 S L6 AND SYNOVITIS?
L15            0 S L14 AND REVIEW/DT
L16           15 S L7 AND SYNOVITIS?
L17            3 S L16 AND REVIEW/DT
L18          291 S L7 AND ARTHRITIS?
L19          100 S L18 AND REVIEW/DT
L20          198 S L7 AND RHEUMATOID () ARTHRIT?
L21           79 S L20 AND REVIEW/DT
L22            2 S L6 AND RHEUMATOID () ARTHRIT?
L23            0 S L22 AND REVIEW/DT
L24            2 S L6 AND GOUT
L25            0 S L24 AND REVIEW/DT
L26           31 S L7 AND GOUT
L27            2 S L26 AND REVIEW/DT

=> s l6 and back () pain
        136209 BACK
          1792 BACKS
        137765 BACK
                  (BACK OR BACKS)
         33624 PAIN
           853 PAINS
         34235 PAIN
                  (PAIN OR PAINS)
           457 BACK (W) PAIN
L28            0 L6 AND BACK (W) PAIN

=> s l7 and back () pain
        136209 BACK
          1792 BACKS
        137765 BACK
                  (BACK OR BACKS)
         33624 PAIN
           853 PAINS
         34235 PAIN
                  (PAIN OR PAINS)
           457 BACK (W) PAIN
L29            6 L7 AND BACK (W) PAIN

=> s l29 and review/dt
       1738344 REVIEW/DT
L30            2 L29 AND REVIEW/DT

=> d l30, ibib abs, 1-2
```

L30 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:149665 HCAPLUS
DOCUMENT NUMBER: 139:300962
TITLE: Clinical pharmacology of etoricoxib: a novel selective **COX-2 inhibitor**
AUTHOR(S): Patrignani, Paola; Capone, Marta L.; Tacconelli, Stefania
CORPORATE SOURCE: Div. Pharmacol., Dep. Med. Cent. Excellence on Aging, 'G. D'Ammunzio' Univ. Sch. Med., Chieti, 66013, Italy
SOURCE: Expert Opinion on Pharmacotherapy (2003), 4(2), 265-284
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with refs. The development of **COX-2 inhibitors** with improved biochem. selectivity (such as etoricoxib and valdecoxib) over that of com. available coxibs has been driven by the potential advantage of safety using higher coxib doses for increased efficacy. Etoricoxib has been approved in the UK as a once-daily medicine for symptomatic relief in the treatment of osteoarthritis (OA), rheumatoid arthritis (RA) and acute gouty arthritis. It is currently approved with addnl. indications (i.e., for relief of acute pain assocd. with dental surgery, for primary dysmenorrhea and for chronic musculo-skeletal pain, including chronic lower-**back pain**) in Mexico, Brazil and Peru. Etoricoxib has an in vitro COX-1/COX-2 IC50 ratio of 344, the highest of any coxib. The administration of therapeutic doses of etoricoxib to healthy subjects does not affect COX1 activity in circulating platelets and gastric biopsies. The profound inhibition of monocyte COX2 activity at 24 h after dosing, as predicted by a pharmacol. half-life of ~ 22 h, supports a once-daily dosing regimen of etoricoxib. In randomized, well-controlled clin. trials, etoricoxib has been shown to have a comparable clin. efficacy with traditional NSAIDs. Combined anal. of efficacy trials with etoricoxib vs. non-selective NSAIDs has shown that the drug halves both investigator-reported upper gastrointestinal perforation, ulcers and bleeds (PUBs) and confirmed PUBs, and reduces the need for gastroprotective agents and gastrointestinal comedications by ~ 40%. The risk of lower extremity edema and hypertension adverse experiences with etoricoxib was low and generally similar to comparator NSAIDs in a combined anal. of eight Phase III studies in OA, RA, chronic low-**back pain** and surveillance endoscopy. Large, randomised clin. trials have been planned to confirm the renal, gastrointestinal and cardiovascular safety of etoricoxib.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:921953 HCAPLUS
DOCUMENT NUMBER: 138:49176
TITLE: Meloxicam (Mobic): a review of its pharmacological and clinical profile
AUTHOR(S): Ogino, Keiko; Saito, Kazushige; Osugi, Takeshi; Satoh, Hisashi
CORPORATE SOURCE: Dep. Pharmacol. Kawanishi Pharma Res. Inst., Nippon Boehringer Ingelheim, Co., Ltd., Kawanishi, 666-0193,

Japan
SOURCE: Nippon Yakurigaku Zasshi (2002), 120(6), 391-397
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review. Meloxicam (Mobic) is a new nonsteroidal anti-inflammatory drug (NSAID) derived from enolic acid, exhibiting selectivity for cyclooxygenase (COX)-2 over COX-1. Meloxicam has shown potent anti-inflammatory and analgesic activity together with low gastrointestinal toxicity in animal models. It is a potent inhibitor not only of acute exudation in adjuvant arthritis in the rat, but also of bone and cartilage destruction. The therapeutic range of meloxicam in the rat, with regard to inhibition of adjuvant arthritis, was several times greater than that of other NSAIDs. Meloxicam in therapeutic doses was found to have no effect on bleeding time or platelet aggregation in healthy volunteers. In clin. studies, meloxicam has shown reliable efficacy against rheumatoid arthritis, osteoarthritis, lumbago (low **back pain**), scapulohumeral periarthritis, and neck-shoulder-arm syndrome with low gastrointestinal toxicity.

```
=> s l6 and inflammat? () sport? () injur?
        180043 INFLAMMAT?
          8464 SPORT?
        130372 INJUR?
             0 INFLAMMAT? (W) SPORT? (W) INJUR?
L31          0 L6 AND INFLAMMAT? (W) SPORT? (W) INJUR?

=> s l6 and sport? () injur?
          8464 SPORT?
        130372 INJUR?
            35 SPORT? (W) INJUR?
L32          0 L6 AND SPORT? (W) INJUR?

=> s l7 and sport? () injur?
          8464 SPORT?
        130372 INJUR?
            35 SPORT? (W) INJUR?
L33          1 L7 AND SPORT? (W) INJUR?

=> s l33 and review/dt
       1738344 REVIEW/DT
L34          1 L33 AND REVIEW/DT

=> d l34, ibib abs, 1

L34  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 1996:512202 HCAPLUS
DOCUMENT NUMBER: 125:184577
TITLE: **COX-2 inhibitors**. Potential for reducing NSAID side-effects in treating inflammatory diseases
AUTHOR(S): Carty, T. J.; Marfat, A.
CORPORATE SOURCE: Central Research Division, Pfizer, Inc., Groton, CT, 06340, USA
SOURCE: Emerging Drugs (1996), 1, 391-411
CODEN: EMDRFV; ISSN: 1361-9195
PUBLISHER: Ashley Publications

DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 82 refs. Downregulation of prostaglandin (PG) formation is essential for the removal of the painful symptoms of inflammation, ranging from **sports injuries** to rheumatoid arthritis. Nonsteroidal anti-inflammatory drugs (NSAIDs, e.g., indomethacin, piroxicam), are well recognized to be clin. efficacious by controlling PG formation through the inhibition of cyclooxygenase (COX), a key enzyme in the PG synthetic cascade. The use of NSAIDs, however, can be limited by their gastrointestinal (GI) and renal side-effects, esp. in the elderly. Recent research has shown that cellular synthesis of PG is derived from two different forms of COX, a constitutive (naturally present) isoform (COX-1) used for the maintenance of organ function (e.g., the GI tract), and an inducible isoform (COX-2) employed for the prodn. of large amts. of PG synthesized during inflammation. Since most NSAIDs inhibit both isoforms, this finding has provided a unique opportunity to discover a pharmacol. agent with specificity for inhibiting COX-2, with little or no effect on COX-1. While retaining the efficacy of conventional NSAIDs, COX-2-selective NSAIDs are expected to display no deleterious effects on the GI tract, thus providing significantly improved toleration. Although it is not clear what their effect will be on the kidney, COX-2-selective agents should offer a pharmacol. profile that predominantly targets PGs produced at the inflammatory site. Should ongoing clin. trials prove the COX-2 concept, this class of compds. could provide a new and exciting generation of anti-inflammatory drugs, which, we would like to propose, could be called COX-2-SAIDs, for COX-2-selective anti-inflammatory drugs.

```
=> s l6 and sprain?
          144 SPRAIN?
L35         1 L6 AND SPRAIN?

=> s l35 and review/dt
      1738344 REVIEW/DT
L36         0 L35 AND REVIEW/DT

=> s l7 and sprain?
          144 SPRAIN?
L37         1 L7 AND SPRAIN?

=> s l37 and review/dt
      1738344 REVIEW/DT
L38         0 L37 AND REVIEW/DT

=> s l6 and strain?
       524784 STRAIN?
L39         3 L6 AND STRAIN?

=> s l39 and review/dt
      1738344 REVIEW/DT
L40         0 L39 AND REVIEW/DT

=> s l7 and strain?
       524784 STRAIN?
L41        15 L7 AND STRAIN?

=> s l41 and review/dt
      1738344 REVIEW/DT
L42         1 L41 AND REVIEW/DT
```

```
=> d l42, ibib abs, 1

L42  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2000:264220  HCAPLUS
DOCUMENT NUMBER:          133:175280
TITLE:                    Apoptosis in the gastric mucosa: molecular mechanisms,
                          basic and clinical implications
AUTHOR(S):                Szabo, I.; Tarnawski, A. S.
CORPORATE SOURCE:         Medical Service, Department of Veterans Affairs
                          Medical Center, Long Beach, Department of Medicine,
                          University of California, Irvine, CA, USA
SOURCE:                   Journal of Physiology and Pharmacology (2000), 51(1),
                          3-15
                          CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER:                Polish Physiological Society
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB    A review, with 71 refs.  Apoptosis a programmed cell death, is an
      essential mechanism of eliminating damaged or aged cells and thus to
      maintain tissue integrity.  There are two central pathways that lead to
      apoptosis: a) the pos. induction by ligands (death factors) binding to
      plasma membrane receptors (death factor receptors) and b) neg. induction
      by the loss of suppressor activity.  The common execution mechanisms of
      apoptosis consist of the activation of cytosolic aspartate-specific
      proteases (ICE-proteases) termed caspases, which can be activated via
      various intracellular pathways.  In the stomach, mucosal surface
      epithelial cells are constantly exfoliating to the gastric lumen and
      completely replaced within 3-5 days under physiol. conditions.  Apoptosis
      has been reported to take place in all regions of the stomach with
      apoptotic cells occurring predominantly in the superficial parts of the
      gastric glands, at a rate of 2-3% for all cells.  Following mucosal injury
      (e.g. ulcer development), apoptosis rapidly increases and remains elevated
      for 2-3 mo.  In a 3-mo old ulcer scar, the apoptosis rate of mucous,
      parietal, chief and endocrine cells was found to be similar to that of
      normal gastric mucosa.  Helicobacter pylori (H. pylori) infection induces
      apoptosis in the gastric mucosa and this action appears to be independent
      of VacA cytotoxin of H. pylori strains.  Nonsteroidal anti-inflammatory
      drugs (NSAIDs), esp. cyclooxygenase-2 (COX-2) inhibitors are potent
      inductors of gastric epithelial cell apoptosis.  However, they can
      abrogate apoptosis or proliferation effects induced by H. pylori.  Many
      details of the exact intracellular and mol. mechanisms regulating
      apoptosis in gastric mucosa remain to be elucidated.
REFERENCE COUNT:          71    THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s l6 and headach?
          7592 HEADACH?
L43          2 L6 AND HEADACH?

=> s l43 and review/dt
       1738344 REVIEW/DT
L44          0 L43 AND REVIEW/DT

=> s l7 and headach?
          7592 HEADACH?
L45         34 L7 AND HEADACH?
```

```
=> s l45 and review/dt
      1738344 REVIEW/DT
L46          10 L45 AND REVIEW/DT

=> d l46,ibib abs, 1-10
```

L46 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:211568 HCAPLUS
DOCUMENT NUMBER: 137:319760
TITLE: An evidence-based evaluation of the gastrointestinal safety of coxibs
AUTHOR(S): Bombardier, Claire
CORPORATE SOURCE: Division of Clinical Decision Making and Health Care, Toronto General Research Institute, Toronto General Hospital, Toronto, ON, Can.
SOURCE: American Journal of Cardiology (2002), 89(6A), 3D-9D
CODEN: AJCDAG; ISSN: 0002-9149
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

Got

AB A review. Nonsteroidal anti-inflammatory drugs (NSAIDs) are nonselective inhibitors of cyclooxygenase (COX) isoforms COX-1 and COX-2. NSAIDs have analgesic and anti-inflammatory properties that are proven, and they are extensively used in the treatment of arthritis, pain, and **headache**. Despite their good efficacy, NSAIDs are assocd. with significant gastrointestinal (GI) toxicity, which appears to be related to the inhibition of the cytoprotective function of COX-1. Thus, selective **COX-2 inhibitors**, or coxibs, were designed to inhibit only the prodn. of COX-2-dependent inflammatory prostaglandins, without any effect on COX-1 and its gastroprotective function. This article reviews important evidence on the GI safety of coxibs. Endoscopic studies demonstrated that coxibs, such as celecoxib and rofecoxib, induced significantly fewer ulcers than nonspecific NSAIDs. To analyze whether the incidence of clin. GI events is also lower with coxibs, 2 large controlled clin. trials, the Celecoxib Long-term Arthritis Safety Study (CLASS) and Vioxx Gastrointestinal Outcomes Research (VIGOR), evaluated the GI safety of celecoxib and rofecoxib, resp. Based on evidence from the VIGOR trial, it was demonstrated that rofecoxib has already fulfilled the promise and significantly decreases the risk of clin. important and complicated GI events compared with a nonselective NSAID, naproxen. In contrast, the CLASS trial showed that the incidence of ulcer complications in patients treated with celecoxib was similar in patients treated with nonspecific NSAIDs.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:649617 HCAPLUS
DOCUMENT NUMBER: 136:79074
TITLE: The coxibs, selective inhibitors of cyclooxygenase-2
AUTHOR(S): Wood, Alastair J. J.; FitzGerald, Garret A.; Patrono, Carlo
CORPORATE SOURCE: Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104-6084, USA
SOURCE: New England Journal of Medicine (2001), 345(6), 433-442

CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review on the development of coxibs as an alternative to nonsteroidal antiinflammatory drugs (NSAID) for treating arthritis, menstrual pain, and **headache**. Both groups of drugs inhibit prostaglandin G/H synthase, the enzyme that catalyzes the transformation of arachidonic acid to a range of lipid mediators, termed prostaglandins and thromboxanes. However, whereas NSAIDs inhibit the two recognized forms of the enzyme, referred to as cyclooxygenase-1 and cyclooxygenase-2, the coxibs are selective inhibitors of cyclooxygenase-2. Since the inhibition of cyclooxygenase-2 has been more directly implicated in ameliorating inflammation, it was hoped that coxibs would be better tolerated than nonselective NSAIDs but equally efficacious.
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:554480 HCAPLUS
DOCUMENT NUMBER: 135:326832
TITLE: The clinical developments and future of the **COX-2 inhibitor** drugs
AUTHOR(S): Goldstein, Jerome
CORPORATE SOURCE: San Francisco Clinical Research Center, San Francisco, CA, 94109, USA
SOURCE: Inflammopharmacology (2001), 9(1-2), 91-99
CODEN: IAOAES; ISSN: 0925-4692
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with refs. A new era of analgesia began with the discovery of aspirin in 1899. Since that time, many newer NSAIDs (non-steroid anti-inflammatory drugs) have been discovered and utilized in clin. practice. The mechanism of anti-inflammatory action of NSAIDs is believed to result from inhibition of the enzyme cyclooxygenase (COX), discovered in the 1970s. This enzyme represents the key rate-limiting step in the prodn. of prostaglandins (PGs) from arachidonic acid. Since PGs are essential for normal gastrointestinal, renal, and platelet function, as well as mediating the inflammatory process, inhibition of cyclooxygenase has both beneficial and deleterious effects. The beneficial effect, obviously, is inhibition of the inflammatory process, while the harmful effects comprise an increased incidence of upper gastrointestinal toxicity (ulceration, perforation, and bleeding) as well as possible renal and platelet dysfunction. In the late 1980s, it was discovered that two isoforms of cyclooxygenase existed (COX-1 and COX-2). COX-1 represents a constitutive form that is expressed in most tissues. In contrast, COX-2 is induced at sites of inflammation and also occurs under normal circumstances in the brain and renal tissues. Since COX-2 levels increase dramatically during acute and chronic inflammation, it was hypothesized that the **COX-2 inhibitors** might offer significant anti-inflammatory qualities with reduced toxicity and may have utility in central nervous system mediated conditions other than peripheral pain, including dementias such as Alzheimer's disease and **headache**, specifically, migraine **headache**.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:466242 HCAPLUS
DOCUMENT NUMBER: 135:282478
TITLE: Rofecoxib: a review of its use in the management of osteoarthritis, acute pain and rheumatoid arthritis
AUTHOR(S): Matheson, Anna J.; Figgitt, David P.
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: Drugs (2001), 61(6), 833-865
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Rofecoxib is a selective cyclo-oxygenase (**COX**)-2 **inhibitor** which has little or no effect on the COX-1 isoenzyme at doses up to 1000 mg/day. Rofecoxib has greater selectivity for COX-2 than celecoxib, meloxicam, diclofenac and indomethacin. In well-controlled clin. trials, rofecoxib 12.5 to 500 mg/day has been evaluated for its efficacy in the treatment of osteoarthritis, acute pain and rheumatoid arthritis [lower dosages (5 to 125 mg/day) were generally used in the chronic pain indications].v. In the treatment of patients with osteoarthritis, rofecoxib was more effective in providing symptomatic relief than placebo, paracetamol (acetaminophen) and celecoxib and was similar in efficacy to ibuprofen, diclofenac, naproxen and nabumetone. Overall, both the physician's assessment of disease status and the patient's assessment of response to therapy tended to favor rofecoxib. In patients with postsurgical dental pain, pain after spinal fusion or orthopedic surgery, or primary dysmenorrhea, rofecoxib provided more rapid and more sustained pain relief and reduced requirements for supplemental morphine use after surgery than placebo. Rofecoxib was more efficacious than celecoxib in patients with acute dental pain and pain after spinal fusion surgery, although celecoxib may have been used at a subtherapeutic dose. In comparison with traditional nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen, diclofenac and naproxen sodium, rofecoxib was similar in efficacy in the treatment of acute pain. Although naproxen sodium provided more rapid pain relief than rofecoxib in patients with primary dysmenorrhea, the reverse was true after orthopedic surgery: rofecoxib provided more rapid pain relief and less supplemental morphine was needed. Rofecoxib was as effective as naproxen in providing symptomatic relief for over 8700 patients with rheumatoid arthritis. Compared with traditional NSAID therapy, rofecoxib had a significantly lower incidence of endoscopically confirmed gastroduodenal ulceration and, in approx. 13 000 patients with osteoarthritis and rheumatoid arthritis, a lower incidence of gastrointestinal (GI) adverse events. Rofecoxib was generally well tolerated in all indications with an overall tolerability profile similar to traditional NSAIDs. The most common adverse events in rofecoxib recipients were nausea, dizziness and **headache**. In conclusion, rofecoxib is at least as effective as traditional NSAID therapy in providing pain relief for both chronic and acute pain conditions. Rofecoxib provides an alternative treatment option to traditional NSAID therapy in the management of symptomatic pain relief in patients with osteoarthritis. Initial data from patients with primary dysmenorrhea and postoperative pain are promising and further trials may confirm its place in the treatment of these indications. Rofecoxib has also shown promising results in patients with rheumatoid arthritis and is likely to become a valuable addn. to current drug therapy for this patient population. Importantly, rofecoxib is assocd. with a lower incidence of GI adverse events than traditional NSAIDs making it a primary treatment option in patients at risk of developing GI complications or patients with chronic

conditions requiring long term treatment.
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2001:349750 HCAPLUS
DOCUMENT NUMBER: 135:220476
TITLE: Nonsteroidal anti-inflammatory drugs in systemic lupus erythematosus
AUTHOR(S): Ostensen, M.; Villiger, P. M.
CORPORATE SOURCE: Department of Rheumatology, Clinical Immunology and Allergy, University Hospital of Berne, Bern, Switz.
SOURCE: Lupus (2001), 10(3), 135-139
CODEN: LUPUES; ISSN: 0961-2033
PUBLISHER: Arnold, Hodder Headline
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 34 refs. Up to 80% of patients with systemic lupus erythematosus (SLE) are treated with nonsteroidal anti-inflammatory drugs (NSAID) for musculoskeletal symptoms, serositis and **headache**. This survey reviews the literature on non-selective and selective inhibitors of cyclooxygenases with an emphasis on the efficacy and safety profile reported in SLE patients. No lupus-specific data on gastro-intestinal side effects of NSAID exist. Both non-selective Cox-inhibitors and selective **Cox-2 inhibitors** induce renal side effects including sodium retention and redn. of the glomerular filtration rate. Lupus nephritis is a risk factor for NSAID-induced acute renal failure, but not for rare idiosyncratic toxic renal reactions to NSAID. In refractory nephrotic syndrome, NSAID have been used successfully. Cutaneous and allergic reactions to NSAID are increased in SLE patients as well as hepatotoxic effects, particularly with high dose aspirin. Whereas a variety of central nervous system side effects of NSAID are probably no more common in SLE patients than in others, aseptic meningitis has been reported more frequently. Ovulation and pregnancy can be adversely affected by Cox-inhibitors. The antiplatelet effect of aspirin and non-selective Cox-inhibitors has a therapeutic potential in patients with the antiphospholipid syndrome (APS). In summary, treatment of SLE with NSAID requires awareness for the increased frequency of some side effects and close monitoring of toxicity.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2001:263605 HCAPLUS
DOCUMENT NUMBER: 135:70473
TITLE: Novel serotonergic and non-serotonergic migraine **headache** therapies
AUTHOR(S): Slassi, Abdelmalik; Isaac, Methvin; Arora, Jalaj
CORPORATE SOURCE: Discovery Chemistry Department, NPS Allelix Corp., Mississauga, ON, L4V 1V7, Can.
SOURCE: Expert Opinion on Therapeutic Patents (2001), 11(4), 625-649
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 196 refs. In the last four years discovery of pharmacotherapeutic treatments for migraine **headaches** has received much attention. Since the patent literature was last reviewed in 1997 [1], advances have been made in the understanding of mechanism and pathophysiol. of migraine. Introduction of sumatriptan to the market has led to acceleration in research efforts towards finding safe and effective treatments for migraine. The importance of this field is evidenced by the no. of compds. in clin. trials and by the no. of patents filed in recent years. For example, besides sumatriptan, a second generation of three new drugs (naratriptan [2], zolmitriptan [3] and rizatriptan [4]) has entered the marketplace and few others are presently in clin. evaluation. In addn., classical drug design has yielded highly potent and selective ligands to target relevant receptor subtypes in migraine treatment. This article highlights and reviews the research advances published in patent literature between Jan. 1997 through Nov. 2000. The article is supplemented with selected refs. on design and development of novel agents with which to treat migraine and to study its mechanism and pathophysiol. Emphasis is made on serotonergic agents, namely serotonin (5-hydroxytryptamine, 5-HT) receptor subtype (5-HT1D, 5-HT1F and 5-HT5) agonists, drug combinations (e.g., 5-HT1D agonists with **COX-2 inhibitors** or NSAIDs), tachykinin receptor (NK1) antagonists and GABAergic agents. Also included are patents describing chem. entities that may be effective in migraine therapy based on their pharmacol. actions as anticonvulsants, LTD4 receptor blocker agents and thromboxane inhibitors. By no means has any attempt been made to exhaustively review the literature; but rather, primary refs. along with citations to latest literature reviews have been included in each section.

L46 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:754174 HCAPLUS
DOCUMENT NUMBER: 134:320365
TITLE: Nonsteroidal anti-inflammatory drugs in systemic lupus erythematosus
AUTHOR(S): Ostensen, M.; Villiger, P. M.
CORPORATE SOURCE: Department of Rheumatology, Clinical Immunology and Allergy, University Hospital of Berne, Bern, CH-3010, Switz.
SOURCE: Lupus (2000), 9(8), 566-572
CODEN: LUPUES; ISSN: 0961-2033
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 60 refs. Up to 80% of patients with systemic lupus erythematosus (SLE) are treated with nonsteroidal antiinflammatory drugs (NSAID) for musculoskeletal symptoms, serositis and **headache**. This survey reviews the literature on non-selective and selective inhibitors of cyclooxygenases, with an emphasis on the efficacy and safety profile reported in SLE patients. No lupus-specific data on gastro-intestinal side effects of NSAID exist. Both non-selective Cox inhibitors and selective **Cox-2 inhibitors** induce renal side effects, including sodium retention and redn. of the glomerular filtration rate. Lupus nephritis is a risk factor for NSAID-induced acute renal failure, but not for rare idiosyncratic toxic renal reactions to NSAID. In refractory nephrotic syndrome, NSAID have been used successfully. Cutaneous and allergic reactions to NSAID are increased in SLE patients as well as hepatotoxic effects, particularly with high dose aspirin. Whereas a variety of central nervous system side effects of NSAID are probably no more common in SLE patients than others, aseptic meningitis has been

reported more frequently. Ovulation and pregnancy can be adversely affected by Cox inhibitors. The antiplatelet effect of aspirin and non-selective Cox inhibitors has a therapeutic potential in patients with antiphospholipid syndrome (APS). In summary, treatment of SLE with NSAID requires awareness for the increased frequency of some side effects and close monitoring of toxicity.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:669180 HCAPLUS
DOCUMENT NUMBER: 132:160652
TITLE: Celecoxib, a selective cyclooxygenase-2 inhibitor for the treatment of rheumatoid arthritis and osteoarthritis
AUTHOR(S): Goldenberg, Marvin M.
CORPORATE SOURCE: Mount Sinai NYU Health, New York, NY, USA
SOURCE: Clinical Therapeutics (1999), 21(9), 1497-1513
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 56 refs. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most frequently prescribed drugs, despite their well-established assocn. with gastroduodenal injury. Recent discovery of the cyclooxygenase (COX) isoenzymes COX-1 and COX-2 has improved our knowledge of the action of NSAIDs. COX-1 is continuously expressed in almost all tissues, where it converts arachidonate to the prostaglandins (PGs) important in homeostatic function; COX-2 is present in immune cells, blood vessel endothelial cells, and synovial fibroblasts. Classic NSAIDs inhibit both COX isoenzymes by occupying the cyclooxygenase-active site, preventing access by arachidonic acid. In theory, a drug such as celecoxib that selectively inhibited COX-2 might block inflammation, pain, and fever while reducing the side effects (gastric erosions and ulcers) assocd. with inhibition of COX-1. In animal models of inflammation and pain, celecoxib has shown marked suppression of PG prodn. and inflammation compared with indomethacin, the std. COX-1/**COX-2 inhibitor**. In clin. trials, celecoxib dosed at 100, 200, and 400 mg BID was found to significantly reduce the signs and symptoms of rheumatoid arthritis (RA) and osteoarthritis. In one RA study, celecoxib was found to be as clin. effective as diclofenac after 24 wk of treatment; at the end of the study, gastroduodenal ulcers occurred significantly more frequently in the diclofenac group (15%) than in the celecoxib group (4%). In a 1-wk endoscopy study comparing celecoxib with naproxen and placebo, the incidence of gastric erosions/ulcers was significantly greater in the naproxen group than in the celecoxib or placebo group. The most common adverse effects of celecoxib in clin. studies were **headache**, diarrhea, abdominal discomfort, and dizziness. Celecoxib has shown significant equiv. anti-inflammatory and analgesic efficacy and has produced less endoscopically apparent gastrointestinal (GI) ulceration or erosion than have 3 classic NSAIDs. Whether it will have long-term GI adverse effects or interact with other medications to cause serious adverse responses (eg, increased GI bleeding or rash in conjunction with other sulfonamide-like drugs) is unknown and remains to be established.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:573219 HCAPLUS
DOCUMENT NUMBER: 131:193552
TITLE: Selective cyclooxygenase-2 inhibitors for the treatment of arthritis
AUTHOR(S): Fung, Horatio B.; Kirschenbaum, Harold L.
CORPORATE SOURCE: Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, USA
SOURCE: Clinical Therapeutics (1999), 21(7), 1131-1157
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 60 refs. The purpose of this paper is to review the rationale for a new class of nonsteroidal anti-inflammatory drugs (NSAIDs) known as selective cyclooxygenase (**COX**)-**2 inhibitors** and to present preliminary clin. data on 2 **COX-2 inhibitors** that are approved for use in the United States. The primary mechanism of NSAIDs in the treatment of inflammation is the inhibition of COX, which exists in 2 forms. COX-1 appears to regulate many normal physiol. functions, and COX-2 mediates the inflammatory response. Theor., an NSAID that inhibits COX-2 selectively should decrease inflammation but not influence normal physiol. functions and thus should cause fewer gastrointestinal side effects. Preliminary data suggest that celecoxib, a highly selective **COX-2 inhibitor**, is superior to placebo and similar to traditional NSAIDs in the short-term treatment of pain due to osteoarthritis, although it has been assocd. with adverse effects such as **headache**, change in bowel habits, abdominal discomfort, and dizziness. Celecoxib also has been shown to be as effective as traditional NSAIDs in the treatment of rheumatoid arthritis, but it may cause fewer adverse effects, including endoscopically documented ulcers. Celecoxib is metabolized in the liver by the cytochrome P 450 isoenzyme CYP2C9, and thus serious drug interactions are possible. In the treatment of osteoarthritis, rofecoxib has been shown to be as effective as traditional NSAIDs and may cause fewer endoscopically documented ulcers, but its complete adverse-effect profile is not known. Until the selective **COX-2 inhibitors** are widely used and more clin. as well as pharmacoeconomic studies are published, the exact role of COX-2 therapy cannot be detd.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:394389 HCAPLUS
DOCUMENT NUMBER: 131:53446
TITLE: Celecoxib: A **COX-2 inhibitor** for the treatment of osteoarthritis and rheumatoid arthritis
AUTHOR(S): Boyce, Eric G.; Breen, Gail A.
CORPORATE SOURCE: Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA, USA
SOURCE: Formulary (1999), 34(5), 405-406,411-414,417
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 18 refs. Celecoxib (Celebrex), a nonsteroidal anti-inflammatory drug (NSAID) indicated for use in osteoarthritis and rheumatoid arthritis, is the first specific cyclooxygenase-2 (**COX-2**)

inhibitor approved by the FDA. By not inhibiting COX-1, celecoxib is expected to have fewer gastrointestinal (Gl) and platelet effects. Celecoxib, which has a sulfonamide component to its chem. structure, is 99% absorbed over 1 to 3 h, 97% protein bound, and extensively metabolized. It has a half-life of 11 h under fasting conditions, which allows once- and twice-daily dosing (200 to 400 mg/day). Celecoxib is a substrate for CYP2C9 and inhibits CYP2D6; both of these features may lead to drug interactions. Celecoxib is as effective as other NSAIDs in the treatment of osteoarthritis and rheumatoid arthritis and superior to placebo. It is assocd. with fewer adverse effects than other NSAIDs, although Gl symptoms and **headaches** are still the most common. Celecoxib may be beneficial for patients at risk for Gl ulcers.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l6 and tendonitis?
            33 TENDONITIS?
L47          0 L6 AND TENDONITIS?

=> s l7 and tendonitis?
            33 TENDONITIS?
L48          0 L7 AND TENDONITIS?

=> s l6 and ankylos?
          1131 ANKYLOS?
L49          2 L6 AND ANKYLOS?

=> s l49 and review/dt
       1738344 REVIEW/DT
L50          0 L49 AND REVIEW/DT

=> s l7 and ankylo? () spondyl?
          1177 ANKYLO?
          1743 SPONDYL?
           847 ANKYLO? (W) SPONDYL?
L51         22 L7 AND ANKYLO? (W) SPONDYL?

=> s l51 and review/dt
       1738344 REVIEW/DT
L52          1 L51 AND REVIEW/DT

=> d l52, ibib abs, 1

L52  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:       2003:46140  HCAPLUS
DOCUMENT NUMBER:        139:172901
TITLE:                  Efficacy and tolerability of meloxicam, a COX-2
                        preferential nonsteroidal anti-inflammatory drug: a
                        review
AUTHOR(S):              Del Tacca, M.; Colucci, R.; Fornai, M.; Blandizzi, C.
CORPORATE SOURCE:       Division of Pharmacology and Chemotherapy, Department
                        of Oncology, Transplants and Advanced Technologies in
                        Medicine, University of Pisa, Pisa, Italy
SOURCE:                 Clinical Drug Investigation (2002), 22(12), 799-818
                        CODEN: CDINFR; ISSN: 1173-2563
PUBLISHER:              Adis International Ltd.
DOCUMENT TYPE:          Journal; General Review
```

LANGUAGE: English

AB A review. Meloxicam is an enolcarboxamide with preferential **COX-2 inhibitory** activity. In vitro studies with human tissues have confirmed the high affinity of meloxicam for COX-2, whereas COX-1 was inhibited only at the highest concns. (ratio of 50% inhibitory concn. for COX-2:COX-1 = 0.09 in whole blood assays). Meloxicam has a bioavailability of 89% after oral administration, is strongly bound to plasma proteins, and its half-life is 20-24 h. It readily penetrates into synovial fluid, reaching 45-57% of plasma concns. Meloxicam pharmacokinetics are not significantly altered in elderly patients or in those with mild renal/hepatic impairment. The efficacy and tolerability of meloxicam in the treatment of pain and inflammation assocd. with rheumatic and musculoskeletal disorders has been evaluated in numerous studies comparing meloxicam 7.5-15 mg/day (up to 22.5 mg/day in **ankylosing spondylitis**), administered for 2 wk to 12 mo, with placebo or other nonsteroidal anti-inflammatory drugs (NSAIDs). Overall, the efficacy of meloxicam was significantly superior to that of placebo and similar to that of other NSAIDs, whereas the incidence of adverse events (esp. gastrointestinal) was lower than with other NSAIDs. I.m. meloxicam provided faster pain relief than the oral drug in patients with rheumatoid arthritis. Meloxicam also appears to be effective in the prevention of post-operative pain, as shown in patients undergoing abdominal hysterectomy or inguinal hernia repair. Meloxicam may also have a cardioprotective role: in patients with acute coronary syndrome without ST-segment elevation, a lower incidence of cardiovascular events was obsd. in those who received meloxicam plus aspirin and heparin vs. aspirin and heparin alone, both during coronary care stay and at 90-day follow-up. Meloxicam has demonstrated a favorable tolerability profile in large-scale comparative trials, where its gastrointestinal tolerability was superior to that of nonselective NSAIDs. In particular, meloxicam 7.5 mg/day was assocd. with a lower incidence of gastrointestinal adverse events compared with diclofenac (13% vs. 19%; $p < 0.001$) or piroxicam (10.3% vs. 15.4%; $p < 0.001$). This was confirmed by a prescription-event monitoring study that found a relatively low incidence of dyspepsia, upper gastrointestinal hemorrhage and peptic ulcer (28.3, 0.4 and 0.3 per 1000 patient-months, resp.) among first-time users of meloxicam. In conclusion, meloxicam is at least as effective as nonselective NSAIDs in the treatment of rheumatic disease or post-operative pain, but has a more favorable gastrointestinal tolerability profile. Further investigations into the potential role of meloxicam as a cardioprotective agent are warranted.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l6 and bursitis?
          131 BURSITIS?
L53         1 L6 AND BURSITIS?

=> s l53 and review/dt
      1738344 REVIEW/DT
L54         0 L53 AND REVIEW/DT

=> s l7 and bursitis?
          131 BURSITIS?
L55         8 L7 AND BURSITIS?

=> s l55 and review/dt
      1738344 REVIEW/DT
L56         0 L55 AND REVIEW/DT
```

```
=> s l6 and dysmenorrhoea?
            21 DYSMENORRHOEA?
L57          0 L6 AND DYSMENORRHOEA?

=> s l7 and dysmenorr?
           749 DYSMENORR?
L58         27 L7 AND DYSMENORR?

=> s l58 and review/dt
       1738344 REVIEW/DT
L59          8 L58 AND REVIEW/DT

=> d l59, ibib abs, 1-8

L59  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2003:875716  HCAPLUS
DOCUMENT NUMBER:          140:35188
TITLE:                    Clinical pharmacology of etoricoxib: a novel selective
                          COX-2 inhibitor. [Erratum to document cited in
                          CA139:300962]
AUTHOR(S):                Patrignani, Paola; Capone, Marta L.; Tacconelli,
                          Stefania
CORPORATE SOURCE:         Div. Pharmacol., Dep. Med. Cent. Excellence on Aging,
                          'G. D'Ammunzio' Univ. Sch. Med., Chieti, 66013, Italy
SOURCE:                   Expert Opinion on Pharmacotherapy (2003), 4(3), 419
                          CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER:                Ashley Publications Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  The data points in Figure 8 were not assigned correctly; the
     cor. figure is given.

L59  ANSWER 2 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2003:149665  HCAPLUS
DOCUMENT NUMBER:          139:300962
TITLE:                    Clinical pharmacology of etoricoxib: a novel selective
                          COX-2 inhibitor
AUTHOR(S):                Patrignani, Paola; Capone, Marta L.; Tacconelli,
                          Stefania
CORPORATE SOURCE:         Div. Pharmacol., Dep. Med. Cent. Excellence on Aging,
                          'G. D'Ammunzio' Univ. Sch. Med., Chieti, 66013, Italy
SOURCE:                   Expert Opinion on Pharmacotherapy (2003), 4(2),
                          265-284
                          CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER:                Ashley Publications Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review with refs.  The development of COX-2 inhibitors with
     improved biochem. selectivity (such as etoricoxib and valdecoxib) over
     that of com. available coxibs has been driven by the potential advantage
     of safety using higher coxib doses for increased efficacy.  Etoricoxib has
     been approved in the UK as a once-daily medicine for symptomatic relief in
     the treatment of osteoarthritis (OA), rheumatoid arthritis (RA) and acute
     gouty arthritis.  It is currently approved with addnl. indications (i.e.,
     for relief of acute pain assocd. with dental surgery, for primary
     dysmenorrhea and for chronic musculo-skeletal pain, including chronic
```

lower-back pain) in Mexico, Brazil and Peru. Etoricoxib has an in vitro COX-1/COX-2 IC50 ratio of 344, the highest of any coxib. The administration of therapeutic doses of etoricoxib to healthy subjects does not affect COX1 activity in circulating platelets and gastric biopsies. The profound inhibition of monocyte COX2 activity at 24 h after dosing, as predicted by a pharmacol. half-life of ~ 22 h, supports a once-daily dosing regimen of etoricoxib. In randomized, well-controlled clin. trials, etoricoxib has been shown to have a comparable clin. efficacy with traditional NSAIDs. Combined anal. of efficacy trials with etoricoxib vs. non-selective NSAIDs has shown that the drug halves both investigator-reported upper gastrointestinal perforation, ulcers and bleeds (PUBs) and confirmed PUBs, and reduces the need for gastroprotective agents and gastrointestinal comedications by ~ 40%. The risk of lower extremity edema and hypertension adverse experiences with etoricoxib was low and generally similar to comparator NSAIDs in a combined anal. of eight Phase III studies in OA, RA, chronic low-back pain and surveillance endoscopy. Large, randomised clin. trials have been planned to confirm the renal, gastrointestinal and cardiovascular safety of etoricoxib.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:621916 HCAPLUS
DOCUMENT NUMBER: 137:163184
TITLE: Valdecoxib (pharmacia)
AUTHOR(S): Gotta, Alexander W.
CORPORATE SOURCE: State University of New York, Brooklyn, NY, 11021-2912, USA
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(2), 240-245
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Pharmacia (formerly Searle), in collaboration with Pfizer and Yamanouchi, has developed valdecoxib, a second generation cyclooxygenase (**COX**)-**2 inhibitor** as a follow-up to celecoxib, for the treatment of arthritis. Pharmacia filed an NDA with the FDA in Mar. 2001 for the treatment of acute pain, **dysmenorrhea**, osteoarthritis (OA) and rheumatoid arthritis (RA). At this time, Pharmacia anticipated a 12-mo review. In June 2001, launch was anticipated in 2002, and in Nov. 2001, valdecoxib was granted FDA approval. The company claims that valdecoxib has improved potency and broader therapeutic range than other **COX-2 inhibitors** including celecoxib, and has the potential for once-daily dosing. By 1999, due to the poor water soly. of valdecoxib, Searle was also developing the prodrug parecoxib. Valdecoxib has been described by Searle as almost superimposable at the site crit. for COX-2 inhibition, a structural side pocket in the enzyme which coincides with the sulfonamide group of the drug. In Apr. 2000, Morgan Stanley Dean Witter estd. sales would be US $400 million in 2003, rising to US $750 million in 2004. In Apr. 2001, Merrill Lynch predicted world sales of US $460 million in 2002, rising to $1065 million in 2005. In Sept. 2000, Merrill Lynch reported that addnl. pain data were being accumulated for this drug, the possible inclusion of which could push filing back to later in the first half of 2001. In May 2001, Merrill Lynch expected launch in 2002. In August 2001, Lehman Brothers predicted that launch would take place in the first half of 2002 and the product would make peak sales of US $1500 million.

Credit Suisse predicted in this month that total sales would reach US $330 million in 2002, rising to US $1832 million in 2004. In Sept. 2001, Morgan Stanley expected launch in the first half of 2002. By Oct. 2001, Credit Suisse had revised its sales predictions to US $180 million in 2002, US $790 million in 2003 and US $1430 in 2004.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:217540 HCAPLUS
DOCUMENT NUMBER: 136:303502
TITLE: Valdecoxib: A **COX-2 inhibitor** for treatment of osteoarthritis, rheumatoid arthritis, and primary **dysmenorrhea**
AUTHOR(S): Goldman, Monica; Schutzer, Steven
CORPORATE SOURCE: Hartford (CT) Hospital, USA
SOURCE: Formulary (2002), 37(2), 68, 71-74, 76-77
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Valdecoxib is a new COX-2-specific inhibitor approved for relief of signs and symptoms of osteoarthritis and adult rheumatoid arthritis and for treatment of primary **dysmenorrhea**. Its **COX-2 inhibitory** potency is equal to that of celecoxib. Although it provides less COX-1 enzyme inhibition than celecoxib, this may not be clin. relevant. Controlled trials have shown valdecoxib to be safe and to provide comparable efficacy to naproxen in arthritis symptom score improvement, redn. of menstruation-assocd. pain, and postoperative analgesia. Valdecoxib has an adverse effect profile similar to that of other **COX-2 inhibitors**, including a gastrointestinal safety benefit over conventional NSAIDs and minimal antiplatelet effects. The risk of reduced renal glomerular filtration rate and acute renal failure appears to be the same as with other **COX-2 inhibitors** and conventional NSAIDs. As with other NSAIDs and **COX-2 inhibitors**, most renal adverse events are a result of sodium retention, peripheral edema, and blood pressure elevation. Valdecoxib has a modest inhibitory effect on metab. of drugs via the cytochrome P 450 3A4, 2C9, 2C19, and 2D6 isoenzymes, but this may not be clin. relevant unless the interacting drug has a narrow therapeutic index. Valdecoxib may be a useful formulary addn. as an alternative to traditional NSAIDs for patients in whom gastrointestinal safety or bleeding is a concern.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:466242 HCAPLUS
DOCUMENT NUMBER: 135:282478
TITLE: Rofecoxib: a review of its use in the management of osteoarthritis, acute pain and rheumatoid arthritis
AUTHOR(S): Matheson, Anna J.; Figgitt, David P.
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: Drugs (2001), 61(6), 833-865
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review. Rofecoxib is a selective cyclo-oxygenase (**COX**)-2 **inhibitor** which has little or no effect on the COX-1 isoenzyme at doses up to 1000 mg/day. Rofecoxib has greater selectivity for COX-2 than celecoxib, meloxicam, diclofenac and indomethacin. In well-controlled clin. trials, rofecoxib 12.5 to 500 mg/day has been evaluated for its efficacy in the treatment of osteoarthritis, acute pain and rheumatoid arthritis [lower dosages (5 to 125 mg/day) were generally used in the chronic pain indications].v. In the treatment of patients with osteoarthritis, rofecoxib was more effective in providing symptomatic relief than placebo, paracetamol (acetaminophen) and celecoxib and was similar in efficacy to ibuprofen, diclofenac, naproxen and nabumetone. Overall, both the physician's assessment of disease status and the patient's assessment of response to therapy tended to favor rofecoxib. In patients with postsurgical dental pain, pain after spinal fusion or orthopedic surgery, or primary **dysmenorrhea**, rofecoxib provided more rapid and more sustained pain relief and reduced requirements for supplemental morphine use after surgery than placebo. Rofecoxib was more efficacious than celecoxib in patients with acute dental pain and pain after spinal fusion surgery, although celecoxib may have been used at a subtherapeutic dose. In comparison with traditional nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen, diclofenac and naproxen sodium, rofecoxib was similar in efficacy in the treatment of acute pain. Although naproxen sodium provided more rapid pain relief than rofecoxib in patients with primary **dysmenorrhea**, the reverse was true after orthopedic surgery: rofecoxib provided more rapid pain relief and less supplemental morphine was needed. Rofecoxib was as effective as naproxen in providing symptomatic relief for over 8700 patients with rheumatoid arthritis. Compared with traditional NSAID therapy, rofecoxib had a significantly lower incidence of endoscopically confirmed gastroduodenal ulceration and, in approx. 13 000 patients with osteoarthritis and rheumatoid arthritis, a lower incidence of gastrointestinal (GI) adverse events. Rofecoxib was generally well tolerated in all indications with an overall tolerability profile similar to traditional NSAIDs. The most common adverse events in rofecoxib recipients were nausea, dizziness and headache. In conclusion, rofecoxib is at least as effective as traditional NSAID therapy in providing pain relief for both chronic and acute pain conditions. Rofecoxib provides an alternative treatment option to traditional NSAID therapy in the management of symptomatic pain relief in patients with osteoarthritis. Initial data from patients with primary **dysmenorrhea** and postoperative pain are promising and further trials may confirm its place in the treatment of these indications. Rofecoxib has also shown promising results in patients with rheumatoid arthritis and is likely to become a valuable addn. to current drug therapy for this patient population. Importantly, rofecoxib is assocd. with a lower incidence of GI adverse events than traditional NSAIDs making it a primary treatment option in patients at risk of developing GI complications or patients with chronic conditions requiring long term treatment.

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:427624 HCAPLUS
DOCUMENT NUMBER: 135:251305
TITLE: Nimesulide: Overview of properties and applications
AUTHOR(S): Rainsford, K. D.
CORPORATE SOURCE: Biomedical Research Centre, Division of Biomedical Sciences, Sheffield Hallam University, Sheffield, S1

1WB, UK
SOURCE: Drugs of Today (2001), 37(Suppl. B, Nimesulide), 3-7
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 11 refs. Nimesulide, a selective cyclooxygenase 2 (**COX-2**) **inhibitor**, has antiinflammatory and analgesic properties. It has a twin arom. ring structure and a relatively high pKa of approx. 6.5. This along with the moderate lipophilicity of nimesulide may confer it low irritant potential, thus allowing for good uptake into the upper gastrointestinal circulation. Like other nonsteroidal antiinflammatory drugs (NSAIDs), nimesulide undergoes phase I metab. via the cytochrome P450 system. The phenolic metabolites undergo phase II metab. to produce phenolic-glucuronides. Nimesulide has been found to have a good safety record esp. in the gastrointestinal tract and is indicated for relief of a variety of conditions involving inflammation and pain, such as osteoarthritis, musculoskeletal conditions and **dysmenorrhea**.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 1999:477373 HCAPLUS
DOCUMENT NUMBER: 131:138671
TITLE: Rofecoxib Merck & Co
AUTHOR(S): Kamali, Farhad
CORPORATE SOURCE: Wolfson Unit of Clinical Pharmacology, University of Newcastle-upon-Tyne, Newcastle-Upon-Tyne, NE1 7RU, UK
SOURCE: Current Opinion in Anti-Inflammatory and Immunomodulatory Investigational Drugs (1999), 1(2), 111-117
CODEN: COAIFF; ISSN: 1464-8474
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 113 refs. Rofecoxib (Vioxx) is a cyclooxygenase-2 (**COX-2**) **inhibitor** under investigation by Merck. An NDA was filed with the US FDA in Nov. 1998 for the indications of osteoarthritis (OA) and pain. In Jan. 1999, the FDA granted a six-month priority review for rofecoxib and in May 1999, the FDA approved rofecoxib for the relief of osteoarthritis, acute pain in adults and treatment of primary **dysmenorrhea**. Vioxx has been launched in the UK for osteoarthritis, and is available in the US, Mexico, Columbia and Peru for the treatment of osteoarthritis, acute pain and primary **dysmenorrhea**. It is also awaiting registration in Canada. Banyu has licensed rofecoxib from Merck, and the drug entered phase II trials, in Japan, in August 1998.
REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 1997:369263 HCAPLUS
DOCUMENT NUMBER: 127:60117
TITLE: Multiple roles of inducible cyclooxygenase-2 and its selective inhibitors
AUTHOR(S): Katori, Makoto; Majima, Masataka

CORPORATE SOURCE: Sch. Med., Kitasato Univ., Sagamihara, 228, Japan
SOURCE: Nippon Yakurigaku Zasshi (1997), 109(6), 247-258
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 43 refs. Cyclooxygenase (COX) is the enzyme that catalyzes the conversion of arachidonic acid to prostaglandin endoperoxides. In addn. to constitutive COX-1, inducible COX-2 has been discovered. COX-2 is induced not only in acute exudative rat carrageenin-induced pleurisy, but in granuloma formation/proliferative inflammation for the acceleration of angiogenesis. This means that COX-2 is induced in the healing process of wounds such as in granuloma of gastric ulcer and the proliferative stage of endometrium. COX-2 is also introduced in ovulation and parturition. Osteoblasts induce COX-2 to accelerate bone absorption. Induction of COX-2 in colon carcinoma is a recent, very exciting topic of investigation. We can learn about many unknown roles of COX-2 from its knockout mouse, but the results must be interpreted cautiously. Development of selective **COX-2 inhibitors**, such as NS-398, opened a new era in which the side effects of gastric and renal lesions by NSAIDs could be ignored. However, prolongation of wound healing by the inhibitors and transient expression of COX-2 must be considered in medical intervention with selective **COX-2 inhibitors**. Nevertheless, acute exudative inflammation, granuloma formation and bone absorption in rheumatoid arthritis are good targets for these inhibitors and application of these inhibitors will be extended to **dysmenorrhea**, interruption of abortion and increasing survival rate of patients with colon carcinoma.

```
=> s l6 and premat? () labor
         28880 PREMAT?
         16171 LABOR
           108 LABORS
         16223 LABOR
                 (LABOR OR LABORS)
           464 PREMAT? (W) LABOR
L60          0 L6 AND PREMAT? (W) LABOR

=> s l7 and premat? () labor?
         28880 PREMAT?
         92954 LABOR?
           464 PREMAT? (W) LABOR?
L61          8 L7 AND PREMAT? (W) LABOR?

=> s l61 and review/t
'T' IS NOT A VALID FIELD CODE
             0 REVIEW/T
L62          0 L61 AND REVIEW/T

=> s l61 and review/dt
       1738344 REVIEW/DT
L63          6 L61 AND REVIEW/DT

=> d l63, ibib abs, 1-6

L63  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2000:405034 HCAPLUS
DOCUMENT NUMBER: 133:129422

TITLE: Nimesulide: some pharmaceutical and pharmacological aspects - an update
AUTHOR(S): Singla, Anil K.; Chawla, M.; Singh, A.
CORPORATE SOURCE: Pharmaceutics Division, University Institute of Pharmaceutical Sciences, Punjab University, Chandigarh, 160 014, India
SOURCE: Journal of Pharmacy and Pharmacology (2000), 52(5), 467-486
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Royal Pharmaceutical Society of Great Britain
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with many refs. Nimesulide, a non-steroidal anti-inflammatory drug (NSAID), is administered orally or rectally twice daily for a variety of inflammation and pain states. This is a unique NSAID, not only because of its chem. structure but also because of its specific affinity to inhibit cyclooxygenase-2 (COX-2), thus exerting milder effects on the gastrointestinal mucosa. Current data on selective **COX-2 inhibitors** suggest that they may have an efficacy similar to that of std. NSAIDs. Initial general clin. experience with selective **COX-2 inhibitors** appears to show that they are particularly promising in individuals at risk because of renal diseases, hypertension or congestive heart failure. Various exptl. models and clin. studies have demonstrated the anti-inflammatory efficacy of nimesulide. Nimesulide is superior, or at least comparable in efficacy, to other NSAIDs, but is better tolerated and has less potential for adverse reactions. Thus, selective **COX-2 inhibitors** should have anti-inflammatory effects devoid of side effects on the kidney and stomach. They may also demonstrate new important therapeutic benefits as anticancer agents as well as help prevention of **premature labor** and even retard the progression of Alzheimer's disease. No clin. significant drug interactions have been reported for nimesulide. Not much has been reported about the pharmaceutical aspects of nimesulide. Its poor aq. soly. poses bioavailability problems in-vivo. This could be overcome by the formation of inclusion complexes with β-cyclodextrin, as has been reported by various researchers. However, absence of any in-vivo data regarding the relative absorption of nimesulide from β-cyclodextrin complex compared with that from conventional formulations of the drug makes the use of such fast-releasing complexes rather questionable. Only a limited no. of assay procedures (HPLC, spectrophotometric, spectrofluorimetric) for the detn. of nimesulide and its metabolite in plasma/urine samples or in dosage forms have been reported in the literature. The purpose of this review is to provide a concise overview of the pharmacol. and pharmaceutical profile of nimesulide. Various investigations carried out recently are reported, although older refs. to research performed on nimesulide have also been included, where appropriate.

REFERENCE COUNT: 150 THERE ARE 150 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:487974 HCAPLUS
DOCUMENT NUMBER: 131:317142
TITLE: Nonsteroidal anti-inflammatory agents
AUTHOR(S): Botting, Jack H.
CORPORATE SOURCE: London, SW16 1UX, UK
SOURCE: Drugs of Today (1999), 35(4-5), 225-235
CODEN: MDACAP; ISSN: 0025-7656

PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 58 refs. Since the synthesis of aspirin in 1897, aspirin-like or nonsteroidal antiinflammatory drugs (NSAIDs) have been the mainstay of therapy for rheumatoid arthritis. Although of diverse chem. structure, these drugs not only exhibit the same antipyretic, analgesic and antiinflammatory therapeutic actions, but they also manifest identical toxic actions on the gastric mucosa and the kidney. This indicated that a single pharmacol. effect was responsible for the properties of NSAIDs, a theory that was confirmed by the epochal discovery by Vane in 1971, that inhibition of the enzyme-producing prostanoids (cyclooxygenase [COX]) produced both the therapeutic and side effects of aspirin-like drugs. However, at equiv. antiinflammatory doses, different NSAIDs exhibited different degrees of toxicity. The reason for this was resolved by the discovery that prostaglandins at sites of tissue damage were synthesized by an inducible COX (COX-2) formed by a gene distinct from that producing the constitutive enzyme (COX-1), responsible for the formation of prostaglandins that serve an essential physiol. function. Modification of the structure of drugs showing a moderately selective effect on COX-2, and the elucidation of the crystal structure of both enzymes, has paved the way for the synthesis of NSAIDs that are highly selective for the inducible enzyme and which are, therefore, antiinflammatory without the typical side effects of the classical NSAIDs. The focus on COX-2 has also expanded our knowledge of the pathophysiol. significance of prostanoids and raised the possibility of new uses for selective **COX-2 inhibitors**, for example, in colon cancer, **premature labor** and possibly Alzheimer's disease. However, the clin. effects of chronic administration of potent, selective **COX-2 inhibitors** must await the results of ongoing clin. trials.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 1998:709445 HCAPLUS
DOCUMENT NUMBER: 129:310297
TITLE: Anti-inflammatory drugs and their mechanism of action
AUTHOR(S): Vane, J. R.; Botting, R. M.
CORPORATE SOURCE: William Harvey Research Institute, St. Bartholomew's Royal London School Medicine Dentistry, Queen Mary Westfield College, London, EC1M 6BQ, UK
SOURCE: Inflammation Research (1998), 47(Suppl.2), S78-S87
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review is given with 113 refs. including a lecture with discussion. Nonsteroidal anti-inflammatory drugs (NSAIDs) produce their therapeutic activities through inhibition of cyclooxygenase (COX), the enzyme that makes prostaglandins (PGs). They share, to a greater or lesser degree, the same side effects, including gastric and renal toxicity. Recent research has shown that there are at least 2 COX isoenzymes. COX-1 is constitutive and makes PGs that protect the stomach and kidney from damage. COX-2 is induced by inflammatory stimuli, such as cytokines, and produces PGs that contribute to the pain and swelling of inflammation. Thus, selective **COX-2 inhibitors** should be anti-inflammatory without side effects on the kidney and stomach. Selective **COX-2 inhibitors** may have other side effects and perhaps other therapeutic potential.

COX-2 (and not COX-1) is thought to be involved in ovulation and in labor. The well-known protective action of aspirin on colon cancer may he through an action on COX-2, which is expressed in this disease. NSAIDs delay the progress of Alzheimer's disease. Thus, selective **COX-2 inhibitors** may demonstrate new important therapeutic benefits as anticancer agents, as well as in preventing **premature labor** and perhaps even retarding the progression of Alzheimer's disease.

L63 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:375493 HCAPLUS
DOCUMENT NUMBER: 129:89714
TITLE: Mechanism of action of anti-inflammatory drugs
AUTHOR(S): Vane, John R.; Botting, Regina M.
CORPORATE SOURCE: The William Harvey Research Institute, St Bartholomew's and the Royal London School of Medicine and Dentistry, Queen Mary and Westfield College, London, ECIM 6BQ, UK
SOURCE: Advances in Experimental Medicine and Biology (1997), 433(Recent Advances in Prostaglandin, Thromboxane, and Leukotriene Research), 131-138
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB As well as benefiting arthritis patients, the new highly selective **COX-2 inhibitors** may demonstrate new important therapeutic benefits, slowing down tumor growth, preventing **premature labor** and perhaps even retarding the progression of Alzheimer's disease. A review with 43 refs.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:262743 HCAPLUS
DOCUMENT NUMBER: 129:22737
TITLE: Mechanism of action of antiinflammatory drugs
AUTHOR(S): Vane, J. R.; Botting, R. M.
CORPORATE SOURCE: The William Harvey Research Institute, St Bartholomew's and the Royal London School of Medicine and Dentistry, Queen Mary and Westfield College, London, ECIM 6BQ, UK
SOURCE: International Journal of Tissue Reactions (1998), 20(1), 3-15
CODEN: IJTEDP; ISSN: 0250-0868
PUBLISHER: Bioscience Ediprint Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 95 refs. In 1971, Vane showed that nonsteroid antiinflammatory drugs (NSAIDs) inhibited the biosynthesis of prostaglandins and proposed this as their mechanism of action. Much work around the world has followed. The aspirin-like drugs inhibit the binding of the prostaglandin substrate, arachidonic acid, to the active site of the enzyme. After characterization of the COX-1 enzyme in 1976, a second COX gene was discovered in 1991 encoding for the inducible COX-2. The constitutive isoform of COX, COX-1, has clear physiol. functions. The inducible isoform, COX-2, is induced by pro-inflammatory stimuli in migratory cells and inflamed tissues. The range of activities of NSAIDs

against COX-1 compared to COX-2 explains the variations in the side effects of NSAIDs at their antiinflammatory doses. Drugs which have the highest potency on COX-2 and less effect on COX- 1 will have potent antiinflammatory activity with fewer side effects. All the results published so far support the hypothesis that the unwanted side effects of NSAIDs, such as damage to the gastric mucosa and kidneys, are due to their ability to inhibit COX-1, while their antiinflammatory (therapeutic effects) are due to inhibition of COX-2. Other roles for **COX-2 inhibitors** will surely be found in the next few years, for prostaglandin formation is under strong control in organs such as the kidney, lungs and uterus. COX-2 is also potently expressed in human colon cancer cells, and NSAIDs delay the progress of colon tumors possibly by causing apoptosis of the tumor cells. The risk of developing Alzheimer's disease, which may involve an inflammatory component, is lessened by chronic ingestion of NSAIDs. The new highly selective inhibitors of COX-2 will not only provide a means of delaying **premature labor** but will also lead to advances in cancer therapy and protection against Alzheimer's disease.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:472427 HCAPLUS
DOCUMENT NUMBER: 127:130327
TITLE: Mechanism of action of aspirin-like drugs
AUTHOR(S): Vane, John R.; Botting, Renia M.
CORPORATE SOURCE: William Harvey Research Institute, St Bartholomew's and Royal London School of Medicine and Dentistry Queen Mary and Westfield College, London, EC1M 6BQ, UK
SOURCE: Seminars in Arthritis and Rheumatism (1997), 26(6, Suppl. 1, Meloxicam: Translating Selective COX-2 Inhibition into Clinical Benefit), 2-10
CODEN: SAHRBF; ISSN: 0049-0172
PUBLISHER: Saunders
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 78 refs. Nonsteroid antiinflammatory drugs (NSAIDs) or aspirin-like drugs act by inhibiting the activity of the cyclooxygenase (COX) enzyme. Two isoforms of COX exist, COX-1, which is constitutively expressed, and COX-2, which is an inducible isoform. Prostaglandins synthesized by the constitutively expressed COX-1 are implicated in the maintenance of normal physiol. function and have a "cytoprotective" action in the stomach. COX-2 expression is normally low but is induced by inflammatory stimuli and cytokines. It is thought that the antiinflammatory actions of NSAIDs are caused by the inhibition of COX-2, whereas the unwanted side effects, such as gastrointestinal and renal toxicity, are caused by the inhibition of the constitutively expressed COX-1. Individual NSAIDs show different selectivities against the COX-1 and COX-2 isoforms. NSAIDs that the selective towards COX-2, such as meloxicam, may have an improved side-effect profile over current NSAIDs. In addn. to their use as antiinflammatory agents in the treatment of rheumatoid arthritis and osteoarthritis, selective **COX-2 inhibitors** may also be beneficial in inhibiting colorectal tumor cell growth and in delaying **premature labor**.

```
=> s l6 and alzheimer? () disease
         30537 ALZHEIMER?
        689983 DISEASE
```

```
        191833 DISEASES
        780229 DISEASE
                  (DISEASE OR DISEASES)
         11951 ALZHEIMER? (W) DISEASE
L64          0 L6 AND ALZHEIMER? (W) DISEASE

=> s l6 and alzheimer?
         30537 ALZHEIMER?
L65          3 L6 AND ALZHEIMER?

=> s l65 and review/dt
       1738344 REVIEW/DT
L66          1 L65 AND REVIEW/DT

=> d l66, ibib abs, 1

L66  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2002:804187  HCAPLUS
DOCUMENT NUMBER:          138:202384
TITLE:                    Oxidative stress in brain aging Implications for
                          therapeutics of neurodegenerative diseases
AUTHOR(S):                Floyd, Robert A.; Hensley, Kenneth
CORPORATE SOURCE:         Free Radical Biology and Aging Research Program,
                          Oklahoma Medical Research Foundation, Oklahoma City,
                          OK, 73104, USA
SOURCE:                   Neurobiology of Aging (2002), 23(5), 795-807
                          CODEN: NEAGDO; ISSN: 0197-4580
PUBLISHER:                Elsevier Science Inc.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review. Age has a powerful effect on enhanced susceptibility to
     neurodegenerative diseases, including susceptibility to stroke and
     cognitive impairment (CI) even in optimally healthy individuals. We
     critically evaluated the notion that oxidative stress increases in aging
     brain. Rigorous studies show logarithmic age-dependent increases in
     oxidized proteins and oxidized DNA lesions. Decreased activity of
     antioxidant protective enzymes does not account for the obsd. increases.
     The reactivity of the lipid oxidn. product 4-hydroxy-2-nonenal (HNE) with
     key mitochondria enzymes may be important in the age-dependent loss in
     energy generation and enhanced susceptibility of neurons to apoptosis.
     Age-dependent enhanced neuroinflammatory processes may play an important
     role in toxin generation that causes death or dysfunction of neurons in
     neurodegenerative diseases. Non-steroidal anti-inflammatory drugs
     (NSAIDs) show significant promise. Vitamin E supplementation did not show
     major beneficial effect on cognitive functions. Major clin. trials for
     Alzheimer's disease (AD) involving cycloxygenase-II (COX II)
     inhibitors and amyloid-beta vaccination have been discontinued. Novel
     therapeutics based on blocking neuron damaging neuroinflammatory processes
     show great promise for abating dementia progression although they have yet
     to make it to clin. practice.
REFERENCE COUNT:          121   THERE ARE 121 CITED REFERENCES AVAILABLE FOR
                                THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                                FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 13:28:27 ON 30 JUN 2004)
```

```
     FILE 'REGISTRY' ENTERED AT 13:28:34 ON 30 JUN 2004
L1             STRUCTURE UPLOADED
L2               3 S L1
L3              52 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:38:30 ON 30 JUN 2004
L4               1 S L3

     FILE 'CAOLD' ENTERED AT 13:38:49 ON 30 JUN 2004
L5               0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:45:22 ON 30 JUN 2004
L6              32 S COX-II () INHIBITOR?
L7            2445 S COX-2 () INHIBITOR?
L8            2447 S L7 OR L6 AND MYOSITIS?
L9            3199 S L7 OR MYOSITIS?
L10             15 S L7 AND MYOSITIS?
L11              0 S L10 AND REVIEW/DT
L12              2 S L6 AND MYOSITIS?
L13              0 S L12 AND REVIEW/DT
L14              2 S L6 AND SYNOVITIS?
L15              0 S L14 AND REVIEW/DT
L16             15 S L7 AND SYNOVITIS?
L17              3 S L16 AND REVIEW/DT
L18            291 S L7 AND ARTHRITIS?
L19            100 S L18 AND REVIEW/DT
L20            198 S L7 AND RHEUMATOID () ARTHRIT?
L21             79 S L20 AND REVIEW/DT
L22              2 S L6 AND RHEUMATOID () ARTHRIT?
L23              0 S L22 AND REVIEW/DT
L24              2 S L6 AND GOUT
L25              0 S L24 AND REVIEW/DT
L26             31 S L7 AND GOUT
L27              2 S L26 AND REVIEW/DT
L28              0 S L6 AND BACK () PAIN
L29              6 S L7 AND BACK () PAIN
L30              2 S L29 AND REVIEW/DT
L31              0 S L6 AND INFLAMMAT? () SPORT? () INJUR?
L32              0 S L6 AND SPORT? () INJUR?
L33              1 S L7 AND SPORT? () INJUR?
L34              1 S L33 AND REVIEW/DT
L35              1 S L6 AND SPRAIN?
L36              0 S L35 AND REVIEW/DT
L37              1 S L7 AND SPRAIN?
L38              0 S L37 AND REVIEW/DT
L39              3 S L6 AND STRAIN?
L40              0 S L39 AND REVIEW/DT
L41             15 S L7 AND STRAIN?
L42              1 S L41 AND REVIEW/DT
L43              2 S L6 AND HEADACH?
L44              0 S L43 AND REVIEW/DT
L45             34 S L7 AND HEADACH?
L46             10 S L45 AND REVIEW/DT
L47              0 S L6 AND TENDONITIS?
L48              0 S L7 AND TENDONITIS?
L49              2 S L6 AND ANKYLOS?
L50              0 S L49 AND REVIEW/DT
L51             22 S L7 AND ANKYLO? () SPONDYL?
L52              1 S L51 AND REVIEW/DT
```

```
L53           1 S L6 AND BURSITIS?
L54           0 S L53 AND REVIEW/DT
L55           8 S L7 AND BURSITIS?
L56           0 S L55 AND REVIEW/DT
L57           0 S L6 AND DYSMENORRHOEA?
L58          27 S L7 AND DYSMENORR?
L59           8 S L58 AND REVIEW/DT
L60           0 S L6 AND PREMAT? () LABOR
L61           8 S L7 AND PREMAT? () LABOR?
L62           0 S L61 AND REVIEW/T
L63           6 S L61 AND REVIEW/DT
L64           0 S L6 AND ALZHEIMER? () DISEASE
L65           3 S L6 AND ALZHEIMER?
L66           1 S L65 AND REVIEW/DT

=> s l7 and alzheimer?
         30537 ALZHEIMER?
L67         96 L7 AND ALZHEIMER?

=> s l67 and review/dt
       1738344 REVIEW/DT
L68         41 L67 AND REVIEW/DT

=> d l68, ibib abs, 1-10

L68  ANSWER 1 OF 41  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2004:299552 HCAPLUS
DOCUMENT NUMBER: 140:331641
TITLE: Novel non-steroidal anti-inflammatory drugs: what we have learned from animal studies
AUTHOR(S): Coruzzi, G.; Menozzi, A.; Dobrilla, G.
CORPORATE SOURCE: Dept. Human Anatomy, Pharmacology and Forensic Medicine, Section of Pharmacology, University of Parma, Parma, Italy
SOURCE: Current Drug Targets: Inflammation & Allergy (2004), 3(1), 43-61
CODEN: CDTICU; ISSN: 1568-010X
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The use of non-steroidal anti-inflammatory drugs (NSAIDs) is frequently assocd. with serious adverse effects related to the inhibition of cyclooxygenase (COX) in tissues where prostanoids exert physiol. effects, such as gastric mucosal defense, renal homeostasis, and platelet aggregation. The discovery of a 2nd COX isoform (COX-2) specifically induced in pathol. tissues led to the development of selective **COX-2 inhibitors**, believed to have an improved safety profile compared to traditional NSAIDs. Animal studies, however, have revealed a protective role for the COX-2 enzyme in the stomach, kidney, heart, vasculature, and reproductive system, and therefore, the safety of COX-2 selective inhibitors needs to be reassessed. On the other hand, new therapeutic indications have emerged as a result of the role played by COX-2 overexpression in cancer or **Alzheimer**'s disease. A 2nd approach aimed at obtaining safer NSAIDs is based on the gastroprotective effects of nitric oxide (NO). Traditional NSAIDs chem. linked to NO-releasing moieties retain the therapeutic efficacy, but not the adverse effects, of the parent NSAIDs. Moreover, addnl. therapeutic applications in cardiovascular diseases, **Alzheimer**'s disease, and cancer were suggested.

PUBLISHER: Kagaku Hyoronsha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review. The topics discussed are (1) prostaglandins (PGs), peroxisome proliferator-activated receptor (PPAR), cyclooxygenase-2 (COX-2) and inflammation; (2) biol. functions of COX-2 in stomach, kidney, brain, platelet, bone, uterus and ovary; (3) **COX-2 inhibitors** as nonsteroidal anti-inflammatory drugs (NSAIDs) in inhibition of PG synthesis; (4) role of COX-2 in rheumatoid arthritis, tumors and **Alzheimer**'s disease; and (5) regulation of COX-2 expression.

L68 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:712759 HCAPLUS
DOCUMENT NUMBER: 140:314103
TITLE: Pharmacology and clinical action of COX-2 selective NSAIDs
AUTHOR(S): Bovill, James G.
CORPORATE SOURCE: Department of Anaesthesiology, Leiden University Medical Centre, Leiden, 2300 RC, Neth.
SOURCE: Advances in Experimental Medicine and Biology (2003), 523(Advances in Modelling and Clinical Application of Intravenous Anaesthesia), 201-214
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, discussing the mol. pharmacol. of cyclooxygenase and some COX-2-selective non-steroidal antiinflammatory analgesics (NSAIDs). The first selective **COX-2 inhibitors**, the coxibs celecoxib, rofecoxib and parecoxib are available for clin. use. Valdecoxib and etoricoxib are currently undergoing clin. trials.
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:710340 HCAPLUS
DOCUMENT NUMBER: 140:2168
TITLE: The structure of mammalian cyclooxygenases
AUTHOR(S): Garavito, R. Michael; Mulichak, Anne M.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Michigan State University, East Lansing, MI, 48824-1319, USA
SOURCE: Annual Review of Biophysics and Biomolecular Structure (2003), 32, 183-206
CODEN: ABBSE4; ISSN: 1056-8700
PUBLISHER: Annual Reviews Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Cyclooxygenases-1 and -2 (COX-1 and COX-2, also known as prostaglandin H2 synthases-1 and -2, resp.) catalyze the committed step in prostaglandin synthesis. COX-1 and -2 are of particular interest because they are the major targets of non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin, ibuprofen, and the new COX-2-selective inhibitors. Inhibition of the COXs with NSAIDs acutely reduces inflammation, pain, and fever, and long-term use of these drugs reduces the incidence of fatal thrombotic events, as well as the development of

Animal data, however, need to be confirmed in large clin. trials. Finally, the increase in endogenous NO via a selective increase in inducible NO synthase in the gastric mucosa is the mechanism underlying the good gastric tolerability and the gastroprotective effects of the non-selective NSAID amtolmetin guacyl, documented to date in the rat.

REFERENCE COUNT: 373 THERE ARE 373 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:969627 HCAPLUS
DOCUMENT NUMBER: 140:399058
TITLE: Experimental brain inflammation and neurodegeneration as model of **alzheimer**'s disease: protective effects of selective **COX-2 inhibitors**
AUTHOR(S): Giovannini, M. G.; Scali, C.; Prosperi, C.; Bellucci, A.; Pepeu, G.; Casamenti, F.
CORPORATE SOURCE: Dipartimento di Farmacologia Preclinica e Clinica "Mario Aiazzi Mancini", Universita di Firenze, Florence, 50139, Italy
SOURCE: International Journal of Immunopathology and Pharmacology (2003), 16(2, Suppl.), 31-40
CODEN: IJIPE4; ISSN: 0394-6320
PUBLISHER: Biolife s.a.s.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Epidemiol. studies indicate that long-term treatment with non steroidal anti-inflammatory drugs reduces the risk of **Alzheimer** Disease and may delay its onset or slow its progression. Neuroinflammation occurs in vulnerable regions of the **Alzheimer**'s disease (AD) brain where highly insol. β-amyloid (Aβ) peptide deposits and neurofibrillary tangles, as well as damaged neurons and neurites, provide stimuli for inflammation. To elucidate the complex role of inflammation in neurodegenerative processes and the efficacy of selective **COX-2 inhibitors** in AD we examd. whether the attenuation of brain inflammatory reaction by selective **COX-2 inhibitors** may protect neurons against neurodegeneration. The data reported in this review show that in in vivo models of brain inflammation and neurodegeneration, the administration of selective **COX-2 inhibitors** prevent not only the inflammatory reaction, but also the cholinergic hypofunction. Our data may help elucidating the epidemiol. findings indicating that anti-inflammatory agents, in particular NSAIDs, reduce the risk of developing AD and may slow its progression.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 3 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:739506 HCAPLUS
DOCUMENT NUMBER: 140:143421
TITLE: Inflammation and COX-2
AUTHOR(S): Sano, Hajime
CORPORATE SOURCE: Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, 663-8501, Japan
SOURCE: Rinsho Men'eki (2003), 39(6), 678-690
CODEN: RNMKAU; ISSN: 0386-9695

DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. A large no. of epidemiol. studies have addressed the possible protective effect of anti-inflammatory drug use with regard to **Alzheimer**'s disease (AD). The most convincing of these studies - the Baltimore Longitudinal Study of Aging - utilized data collected prospectively, thereby minimizing recall bias issues. However, despite this evidence, therapeutic studies investigating nonsteroidal anti-inflammatory drugs (NSAIDs), including cyclooxygenase-1 (COX-1) and **COX-2 inhibitors** and steroids, do not support this hypothesis. This discrepancy may be due to the fact that the bulk of epidemiol. evidence has examd. the likely incidence of AD prior to the onset of clin. symptoms of disease. On the basis of this information, the article will attempt to formulate a possible scenario, in which optimal NSAIDs might be tested in the most favorable clin. therapeutic conditions in order to det. whether NSAIDs can provide beneficial treatment for the clin. progression of AD dementia.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 8 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2002:804187 HCAPLUS
DOCUMENT NUMBER: 138:202384
TITLE: Oxidative stress in brain aging Implications for therapeutics of neurodegenerative diseases
AUTHOR(S): Floyd, Robert A.; Hensley, Kenneth
CORPORATE SOURCE: Free Radical Biology and Aging Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA
SOURCE: Neurobiology of Aging (2002), 23(5), 795-807
CODEN: NEAGDO; ISSN: 0197-4580
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Age has a powerful effect on enhanced susceptibility to neurodegenerative diseases, including susceptibility to stroke and cognitive impairment (CI) even in optimally healthy individuals. We critically evaluated the notion that oxidative stress increases in aging brain. Rigorous studies show logarithmic age-dependent increases in oxidized proteins and oxidized DNA lesions. Decreased activity of antioxidant protective enzymes does not account for the obsd. increases. The reactivity of the lipid oxidn. product 4-hydroxy-2-nonenal (HNE) with key mitochondria enzymes may be important in the age-dependent loss in energy generation and enhanced susceptibility of neurons to apoptosis. Age-dependent enhanced neuroinflammatory processes may play an important role in toxin generation that causes death or dysfunction of neurons in neurodegenerative diseases. Non-steroidal anti-inflammatory drugs (NSAIDs) show significant promise. Vitamin E supplementation did not show major beneficial effect on cognitive functions. Major clin. trials for **Alzheimer**'s disease (AD) involving cycloxygenase-II (COX II) inhibitors and amyloid-beta vaccination have been discontinued. Novel therapeutics based on blocking neuron damaging neuroinflammatory processes show great promise for abating dementia progression although they have yet to make it to clin. practice.
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 9 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:795379 HCAPLUS
DOCUMENT NUMBER: 138:313675
TITLE: From cyclooxygenase activities to **Alzheimer**'s disease neuropathology: experimental approaches and therapeutic interventions
AUTHOR(S): Pasinetti, Giulio Maria
CORPORATE SOURCE: Neuroinflammation Research Laboratories, Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, 10029, USA
SOURCE: Drug Development Research (2002), 56(3), 438-445
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Several prospective and retrospective epidemiol. studies have demonstrated a protective effect for antiinflammatory drugs in **Alzheimer**'s disease (AD). However, despite this evidence therapeutic studies investigating nonsteroidal antiinflammatory drugs (NSAIDs), including cyclooxygenase (COX)-1 and **COX-2 inhibitors** and steroids, do not support this hypothesis. This discrepancy may be due to the fact that the bulk of epidemiol. evidence has examd. the likely incidence of AD prior to the onset of clin. symptoms of disease. In contrast, in therapeutic studies NSAIDs are administered to patients with illnesses severe enough to exceed the clin. detection threshold, suggesting that NSAID therapy administered following the onset of AD may not be optimally effective. Thus, patients at high risk for AD, e.g., those with mild cognitive impairment (MCI), may be more suitable for study in clin. trials of NSAIDs. Indeed, recent evidence suggests that different indexes of classical inflammatory cascades have distinct assocns. with different phases of the clin. progression of AD. In this review, I discuss the potential role of inflammation in the clin. progression of AD and how this evidence relates to preventive use of antiinflammatory drugs for AD treatment. I then examine the importance of evidence for the potential role of inflammation in amyloidosis in the AD brain and exptl. models. I consider the implications of inflammation in AD and recent evidence potentially supporting a neg. role of inflammation in vaccination therapy trials. In conclusion, I examine cutting-edge clin. studies investigating NSAID therapy for AD.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 10 OF 41 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:762780 HCAPLUS
DOCUMENT NUMBER: 138:247857
TITLE: Pain management and beyond: evolving concepts and treatments involving cyclooxygenase inhibition
AUTHOR(S): Staats, Peter S.
CORPORATE SOURCE: Department of Anesthesiology and Critical Care Medicine, Division of Pain Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: Journal of Pain and Symptom Management (2002), 24(1S), S4-S9
CODEN: JPSMEU; ISSN: 0885-3924
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review. Chronic uncontrolled pain may be the greatest health care crisis facing the United States. It is the major symptom for which patients seek medical care and is assocd. with substantial economic and psychosocial costs. For many patients, particularly the elderly and those suffering from cancer, chronic pain is often undertreated. Because pain has an emotional component and is frequently accompanied by depression and/or anxiety, patients benefit from a comprehensive assessment and multidisciplinary approach to treatment. It is likely that coxibs (cyclooxygenase or COX-2-selective inhibitors) will assume an increasingly prominent role in the treatment of chronic pain assocd. with arthritis, cancer, and other diseases either as monotherapy or in combination with other drugs. In addn., the role of COX-2 inhibition in the prevention and treatment of colon cancer, **Alzheimer**'s disease (AD), and other chronic health problems is an area currently undergoing intense investigation.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>